SCIENCE

10 August 1956

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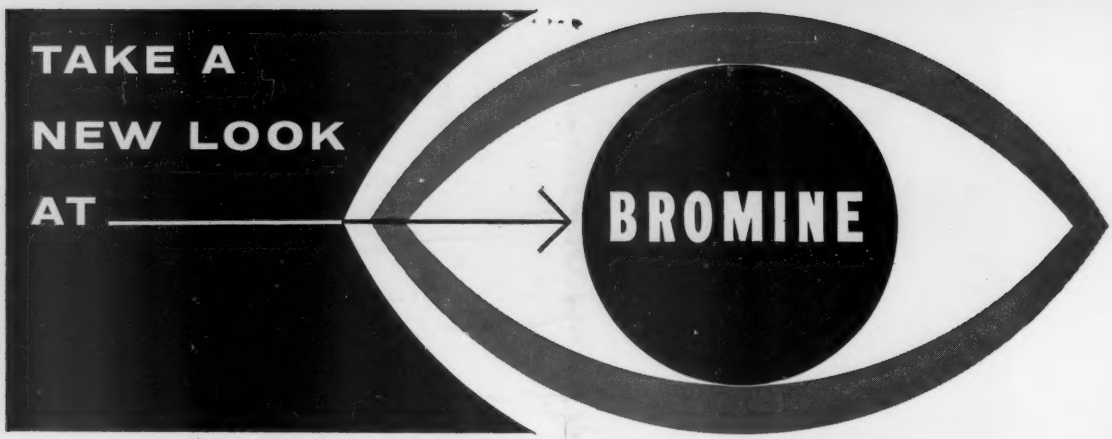

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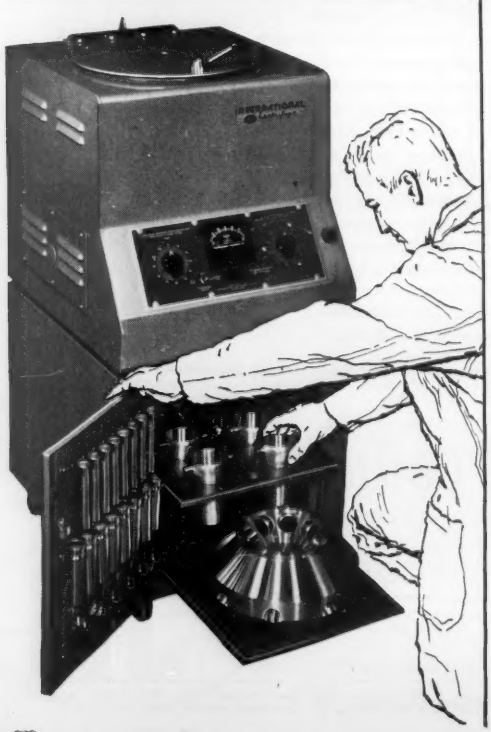

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10 August 1956, Volume 124, Number 3215

SCIENCE

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"Letters" in *Science*

With this issue we are reinstating a section that, under various titles, was a feature of *Science* from the first issue on 9 February 1883 till 24 June 1955. The section began under the title "Letters to the Editor," but even in the first issue it included a note that might better have been described as a technical paper. The section continued to include short technical papers when, a few years later, its title was changed to "Discussion and Correspondence." In 1903 technical papers were put in a new section, "Shorter Articles," thus achieving a nominal separation of letters and technical papers. This last section has at various subsequent times been called "Special Articles" and "Technical Papers." It is represented in recent issues by "Reports" in the "Reports and Letters" section. The various editors have exercised similar semantic ingenuity in titling the letters section. It has appeared not only under the two titles already mentioned but also as "Discussion," "Comments by Readers," "Comments and Communications," and "Communications."

A sampling of the section devoted to comments, under whatever title, shows that short technical papers were regularly included and indeed, before the recent fusion of the two sections, short technical papers were published rapidly in this section, while longer papers were published somewhat more slowly as "Technical Papers."

A rough and ready analysis of the 105 notes (or articles or letters) included in the last volume in which they were separated from technical papers shows that letters (that is, opinion and comment) totaled only 32, the remaining 73 being technical papers and descriptions of methods or apparatus.

It was doubtless the blurring of the distinction between the two sections that led to their fusion in July 1955. Our proposal to set up a letters section again stems from our view that a forum for the expression of comment and opinion will make a desirable addition to the journal and from our hope that the distinction between letters and reports can be more sharply drawn than in the past. Technical papers and technical letters commenting upon them will be published as "Reports." Letters that comment on something that has appeared in other sections of *Science* and expression of opinion—including critical opinion—will be published as "Letters."

We propose the following ground rules for "Letters." Letters will be neither acknowledged nor returned; authors will receive neither proof nor an opportunity to obtain reprints; anonymous letters will be disregarded; the editors will reserve the right to make deletions; letters of not more than 250 words will be preferred; the editors' decision about whether or not to publish letters will be final and not subject to continuing correspondence; an author should indicate whether or not his letter is intended for publication; letters should be typed doubled spaced and submitted in duplicate; as is usual in a section of this kind, the editors will take no responsibility for the accuracy or soundness of the letters published.

So much for the rules, except to add that experience will doubtless teach us that some should be modified and that others, not at present contemplated, will have to be devised, if the section is to play the part we hope it will in making *Science* more useful, more interesting, and more informative.—G. DUS.

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Radioactive Fallout through September 1955

Merril Eisenbud and John H. Harley

Soon after the fallout-monitoring network of the U.S. Atomic Energy Commission was established in the United States, it became apparent that daily fallout observations could be made by simple procedures at great distances from a nuclear detonation, and the network was expanded in October 1952 to include a number of locations beyond the continental United States. Additional stations were again added in February 1954, and since then the sampling program has been conducted at 88 stations, including 26 in the United States. These operate continuously. Additional stations in the United States are added when nuclear detonations are being conducted in Nevada. The overseas stations are listed in Table 1, the continental stations in Table 2.

The data collected within continental United States through August 1954 have been reported in previous publications (*1*, *2*). In this report (*3*) are summarized the data obtained in the United States and abroad through September 1955.

The principal objective of the monitoring program is to enable one to estimate the levels of human exposure produced by radioactive fallout at great distances from nuclear detonations. Such exposure may result from external irradiation by radioactive dust deposited on the surface of the earth or from internal irradiation by specific radionuclides that enter the body by ingestion.

With respect to ingestion, strontium-90 is the nuclide selected for continuing attention because, from the point of view of the long-range behavior of the isotopes involved in biological systems, it is potentially the most hazardous. This is due in part to its relatively long half-life (about 28 years) but, more particularly, because of the chemical similarity of strontium to calcium and the possibility that strontium-90 can therefore be assimilated into biological processes involving calcium and ultimately be deposited in human bone.

The data from the monitoring network provide the following estimates for each place where a station is located. (i) The cumulative surface deposits of mixed fission products and strontium-90. These estimates are reported in millicuries per square mile. (ii) The cumulative gamma dose (in millirads) from external radiation.

It will be noted that the earlier publications did not include estimates of the gamma dose. However, in recognition of the increased interest in such estimates, these data have been computed for the full sampling period and will hereafter be available on a continuing basis.

Method of Sampling

Adhesive-coated films, as described previously, are used for collecting samples. An adhesive coated acetate film is supported horizontally on a frame about 3 feet above the ground. The coating retains its adhesive properties when it is wet, and the radioactive dust particles that are entrapped in raindrops are collected, possibly by impaction against the adhesive surface. Most stations maintain duplicate sampling units, thus providing some assurance against loss of samples. The films are changed each day at the same time and are mailed to the U.S. Atomic Energy Commission Health and Safety Laboratory in New York, where their radioactivity is assayed.

Studies have continued of the collection characteristics of gummed film in comparison with those of high-walled pots. Analyses of the data have been completed for an 84-week test period, indicating that the gummed film is 63 percent efficient if we make the assumption that the high-walled pots collect total fallout. We consider that the pots provide the best practical estimate of total fallout, and the data obtained from the use of gummed films have therefore been corrected by a factor of 1.6.

Methods of Estimation

Mixed fission product activity. When the sample is received in the laboratory, it is ashed at 550° to 600°C, and its beta activity is counted. The potassium-40 activity of a known weight of potassium carbonate is used as the basis for converting counts per minute to millicuries. This activity is then calculated as of (i) the sampling day and (ii) an arbitrary future date, usually the first day of the following calendar year. These extrapolations depend on knowledge of the age of the sample, its decay being assumed to be proportional to $t^{-1.2}$. At any given time, the sum of the extrapolated daily values provides an estimate of the cumulative radioactivity deposited at the sampling station as of the arbitrary date.

Strontium-90. The strontium-90 content of the samples can be estimated from Hunter and Ballou curves of relative isotopic abundance (*4*), or they can be measured directly by radiochemistry. When the latter procedure is used, it is desirable to collect the samples for a period of at least 1 month to facilitate the counting procedures, and a suitable vessel such as a high-walled pot can be exposed for this purpose.

The Hunter and Ballou curves were used during this reporting period.

Gamma dose. It is not possible to measure directly the cumulative gamma dose from fallout at a distance from a nuclear detonation. The normal gamma-radiation background of cosmic and terrestrial origin is much larger in magnitude than the gamma radiation from fallout, and usually masks the latter completely. It is

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thus necessary to estimate the cumulative gamma dose by indirect means.

In calculating the dose, it has been assumed that the daily fallout is deposited uniformly on an infinite smooth plane, where it remains to infinite time. The integrated infinite dose for each daily fallout is calculated from the measured beta activity, using the known isotopic composition of the sample and the known gamma characteristics. The sum of these integrated infinite doses from each of the daily samples collected during any given time represents the estimated gamma dose for infinite time delivered to populations who are exposed from the start of the sampling period. For practical estimates, the infinite dose is delivered in 2 to 4 years after fallout.

The integrated gamma dose is sensitive to the time of fallout, particularly in those parts of the world in which fallout may occur within 1 or 2 days of the detonation. In such cases, the bulk of the gamma dose is delivered within 1 month or so after fallout. It is thus desirable to know the time of fallout, at least to the nearest day, and for this reason daily samples are collected.

The United States collections were begun on a systematic basis in the fall of 1951. However, because of the way in which the data were organized prior to the fall of 1952, it has not proved practical to calculate the gamma dose estimates prior to this date. An exception has been made in Salt Lake City, Utah, which is the only location beyond the immediate vicinity of the Nevada test site known to have received a gamma dose during this period that is significant in relation to the total received since October 1952.

Table 1. Fallout at stations outside continental United States, October 1952 to September 1955. Stations that have not sampled continuously since October 1952 are indicated by an asterisk.

Station	Mixed fission products (mc/mi²)	Strontium-90 (mc/mi²)	Gamma dose (mrad)
1. Anchorage, Alaska	62	2.7	6.5
2. Edmonton, Alberta	78	2.8	7.6
3. Regina, Saskatchewan	82	3.0	9.3
4. Winnipeg, Manitoba	95	3.6	14
5. Churchill, Manitoba	50	1.9	4.1
6. Moosoonee, Ontario	67	2.8	12
7. North Bay, Ontario	100	3.1	12
8. Ottawa, Ontario	110	3.4	12
9. Montreal, Quebec	110	4.0	13
10. Seven Islands, Quebec	84	3.3	12
11. Moncton, New Brunswick	83	3.7	10
12. Goose Bay, Labrador*	160	4.0	13
13. Stephenville, Newfoundland	120	4.3	18
14. Thule, Greenland	50	2.0	3.6
15. Keflavik, Iceland	92	2.9	8.1
16. San Juan, Puerto Rico*	100	3.9	14
17. Bermuda	96	4.6	19
18. Mexico City, Mexico	110	5.1	22
19. San Jose, Costa Rica	63	3.2	11
20. Panama Canal Zone	89	4.1	15
21. Bogota, Colombia	50	2.6	10
22. Quito, Ecuador	51	2.6	10
23. Lima, Peru	50	1.8	5.0
24. La Paz, Bolivia	92	4.2	14
25. Belem, Brazil	74	3.4	12
26. São Paulo, Brazil	53	2.7	9.7
27. Buenos Aires, Argentina	60	2.8	9.4
28. Prestwick, Scotland	87	3.8	7.9
29. Oslo, Norway*	56	2.5	6.2
30. Rhein Main, Germany	100	3.5	9.0
31. Sidi Slimane, Morocco*	64	2.5	6.6
32. Tripoli, Libya	83	4.0	12
33. Dakar, French West Africa	74	3.6	8.0
34. Lagos, Nigeria*	33	1.9	4.6
35. Leopoldville, Belgian Congo*	70	3.4	8.0
36. Addis Ababa, Ethiopia*	110	4.2	10
37. Pretoria, Union of South Africa	39	2.0	4.2
38. Durban, Union of South Africa*	34	1.9	4.9
39. Colombo, Ceylon*	91	4.7	23
40. Singapore, Malaya*	95	4.6	18
41. Misawa, Japan*	73	2.8	9.6
42. Tokyo, Japan*	100	3.8	13
43. Hiroshima, Japan	66	3.2	11
44. Nagasaki, Japan*	92	4.9	16
45. Kadena, Okinawa*	76	4.0	14
46. Taipei, Taiwan*	100	4.6	16
47. Manila, Philippine Islands*	110	6.6	29
48. Iwo Jima*	290	24	150
49. Yap, Caroline Islands*	170	9.0	40
50. Guam, Caroline Islands	160	8.5	40
51. Truk, Caroline Islands*	190	9.2	47
52. Ponape, Caroline Islands*	240	14	63
53. Wake Island*	89	3.6	13
54. Noumea, New Caledonia*	60	3.2	12
55. Sydney, Australia*	65	3.5	12
56. Melbourne, Australia*	47	2.1	6.6
57. Wellington, New Zealand*	40	2.1	6.4
58. Honolulu, Hawaii	83	3.5	15
59. Johnston Island*	130	5.9	28
60. Canton Island*	86	4.2	19
61. Dhahran, Saudi Arabia*	57	3.1	7.9
62. Beirut, Lebanon*	73	3.3	8.4

Findings

The cumulative mixed fission product data as of 1 January 1956 are summarized on the world-wide map in Fig. 1, and strontium-90 and gamma dose data are given in Table 1. The United States data are listed individually in Table 2.

The estimates of mixed fission products and strontium-90 in the United States include the period from October 1951 to September 1955. Although some of the foreign stations began collections in October 1952, not all of them have sampled continuously since that time; these are indicated by an asterisk. Full data are available from the Pacific and Asian locations for the 1952 and 1954 Pacific tests, but they are not always available during 1953, when a Nevada test series was conducted. Some of the European, African, and South American stations did not collect samples during the Pacific test series in 1952. The missing data at these foreign stations have been estimated by regional interpolation. All stations have been sampling continuously since 1 January 1954, and it is since that time that the bulk of the fallout to date has occurred at most overseas stations.

The gamma doses, which are derived by calculation from the fallout of mixed fission products, are not available prior

to October 1952 for any United States stations except Salt Lake City. However, the values reported may be taken as a satisfactory approximation of the total gamma dose delivered to date. The fallout prior to October 1952 was of a low order compared with that during the subsequent period.

As expected, the high accumulations of mixed fission products (Fig. 1) exist in the vicinity of the proving grounds in Nevada and in the vicinity of the Pacific test area. The highest recorded deposition, Grand Junction, Colo., is 740 millicuries per square mile as of 1 January 1956. The values are lower everywhere else, the next highest deposition being 290 millicuries per square mile at Iwo Jima in the Western Pacific Ocean. The lowest value is Lagos, Nigeria, with 33 millicuries per square mile. In general, the mixed fission products data are characterized by a high degree of regional uniformity in which, with few exceptions, adjacent stations agree within ± 50 percent.

The estimates of strontium-90 are shown in Tables 1 and 2. Outside of the United States, the observed range is from 1.8 millicuries per square mile in Peru to 24 millicuries per square mile at Iwo Jima. In the United States, the accumulation varies from 2.1 at San Francisco to 23 at Salt Lake City. For most of the world covered by this network, the range of 2 to 5 millicuries per square mile may be taken as a representative estimate of the distribution of strontium-90.

With respect to the gamma dose, the average value for the United States is higher than it is for the rest of the world. The range of values in the United States is relatively narrow, 6 to 49 millirads, except for Salt Lake City (160), Grand Junction (120), and Albuquerque, N.M. (110). The representative dose for eastern United States is about 15 to 20 millirads, with slightly higher values in the Middle West and lower values on the West Coast.

The cumulative gamma dose at the foreign stations is in the range of 4 to 23 millirads, except for some of the Pacific islands, where the range is from 13 to 150 millirads.

These gamma values are somewhat lower than the average estimate of 100 milliroentgens for the United States as reported by Dunning (*5*) whose calculation was intended to provide a tentative upper limit of the estimated dose and was deliberately conservative.

Table 2. Fallout at stations within continental United States, October 1951 to September 1955.

Station	Mixed fission products (mc/mi²)	Sr^{90} (mc/mi²)	Gamma dose* (mrad)
Albuquerque, N.M.	400	20	110
Atlanta, Ga.	120	3.8	16
Billings, Mont.	160	5.7	24
Binghamton, N.Y.	61	2.2	7.8
Boise, Idaho	160	9.2	16
Chicago, Ill.	140	5.3	24
Dallas, Tex.	170	6.1	29
Des Moines, Iowa	170	6.2	28
Detroit, Mich.	140	4.2	21
Grand Junction, Colo.	740	18	120
Jacksonville, Fla.	88	3.3	13
Memphis, Tenn.	200	8.4	49
Minneapolis, Minn.	130	4.9	18
New Haven, Conn.	110	3.6	17
New Orleans, La.	170	5.7	27
New York, N.Y.	110	4.2	17
Philadelphia, Pa.	110	4.6	16
Pittsburgh, Pa.	100	4.1	13
Rapid City, S.D.	150	6.1	25
Rochester, N.Y.	99	3.7	13
St. Louis, Mo.	200	6.0	27
Salt Lake City, Utah	680	23	160
San Francisco, Calif.	47	2.1	5.8
Seattle, Wash.	89	3.5	11
Scottsbluff, Neb.	200	6.3	26
Washington, D.C.	86	3.0	11

* Gamma dose for the period October 1952 to September 1955, except for Salt Lake City, which covers the period October 1951 to September 1955.

Discussion

The collection efficiency of the gummed film is of fundamental importance in interpreting reported values. As noted previously, the over-all efficiency for collection of total fallout activity is taken to be 63 percent, and all of the data have been corrected accordingly.

A source of error which is more difficult to assess is that inherent in the assumption that the decay of the radioactivity is proportional to $t^{-1.2}$. Application of this decay law requires that the age of the debris be known with some certainty, and this has become increasingly difficult during the past 2 years. Prior to 1954, it was possible to predict the decay characteristics of a sample accurately because at any given time the debris was known to have originated from the most recent test series. After each series, the daily fallout would diminish rapidly and would ordinarily be undetectable before the next series of tests started.

The rapid diminution in fallout from tests conducted prior to the spring of 1954 can be explained by the fact that, except for Operation Ivy in November 1952, the yields from detonations were relatively low, and the bulk of the debris was distributed below the tropopause, where fallout is greatly hastened by precipitation and other factors. In contrast, the detonation of devices having yields equivalent to megatons of TNT produces clouds of radioactive debris which pierce the tropopause and become distributed in the stratosphere. From this relatively stable region of the earth's atmosphere, the particles descend slowly, and fallout to the earth's surface occurs over a period of time which is measured in years rather than weeks or months. The traces of relatively old debris from high-yield devices become mixed with the debris of subsequent detonations. This being the case, neither the decay characteristics of a sample nor the relative abundance of the long-lived isotopes can be predicted from theory.

In recent months, the procedure has been changed and, where necessary, either individual or pooled samples are followed for decay.

There is no practical way in which the accuracy of the estimates of accumulated mixed fission products can be tested experimentally. However, it is possible to test the validity of the strontium-90 estimates by direct radiochemical analyses of the soils from the vicinity of the sampling stations. In October 1955, immediately following the sampling period covered by this report, soil samples were collected from 17 widely scattered locations in the United States. The relationships between the predicted and measured values are given in Figure 2. It is seen that the data consist of two groupings, in which 14 points show a reasonably satisfactory regression of measured on predicted values. The correlation coefficient for these data is 0.70. The other three points for stations near the Nevada test site show low ratios

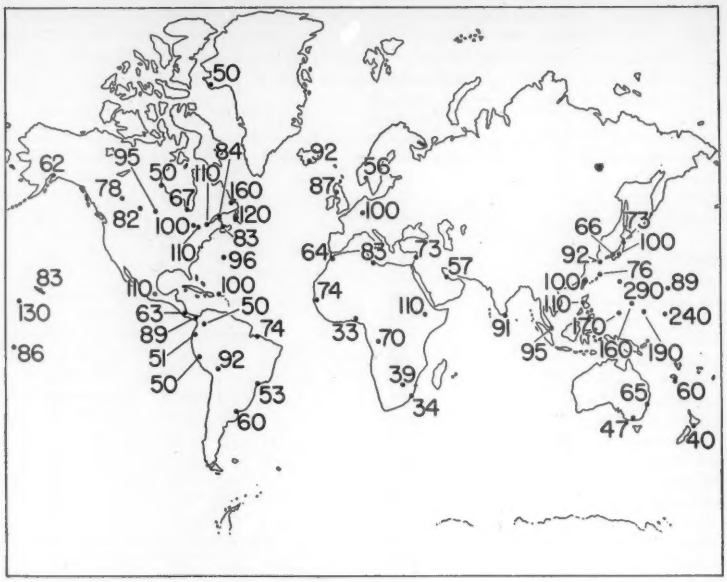

Fig. 1. Cumulative deposition of mixed fission products in millicuries per square mile at the stations shown. These data are for fallout from October 1952 to September 1955 and are extrapolated to 1 January 1956.

of measured to predicted strontium-90.

These findings are consistent with present knowledge of the way strontium-90 is formed and distributed. The estimates of strontium-90 were obtained by using the Hunter and Ballou curves of relative isotopic abundance in conjunction with the daily measurement of mixed fission products. Because strontium-90 is derived following fission from its precursor krypton-90, an inert gas which has a half-life of 33 seconds, some of the strontium-90 is formed relatively late in the life of the fireball. The relative abundance of strontium-90 in any given particle of dust is variable—there is a depletion of strontium-90 in debris which falls out relatively close to the site of detonation and a corresponding enrichment from debris which falls out at greater distances. This may explain the low ratios of measured-to-predicted values for Albuquerque, Salt Lake City, and Grand Junction, which are relatively close to the Nevada site. Similarly, fallout analyzed at great distances from detonations is known to be enriched in strontium-90 by as much as a factor of 2, which explains why the measured values at the other stations were higher than the predicted values. Based on this soil study, one might be justified in doubling the strontium-90 values given, but this factor was not used in preparing the tables.

The estimates of gamma dose, like the estimates of strontium-90 were derived by calculations from estimates of the fallout of mixed fission products. It should be noted that the assumptions underlying the calculation of gamma dose tend to produce values which are much higher than the doses to which populations are actually exposed. The reported values do not allow for weathering or shielding.

The effects of weathering and shielding cannot be treated quantitatively. For populations in cities, the true dose would be very much reduced by the fact that fallout to the surface is soon washed into gutters and storm sewers. For these reasons, it is likely that the actual dose to urban populations does not exceed 10 percent of the values reported here.

Rural populations are less shielded by buildings and do not have the advantage of large paved areas to encourage runoff during storms. Nevertheless, the true situation is never the infinite smooth plane on which these calculations are based, and some reduction is afforded by irregularities in the terrain, the plowing of fields, and other factors.

Significance of Findings

In interpreting the significance of these data, one needs to consider only the estimates of gamma dose and distribution of strontium-90. The total accumulations of mixed fission products are important only insofar as they serve as the basis for estimating the gamma dose delivered and the amount of strontium-90 present.

Geneticists are concerned with the average gamma dose to populations because this serves as the basis for estimating the number of radiation-induced chromosome mutations in the population as a whole. By referring to the tables, the average dose may be taken to be in the order of 10 millirads for the 4-year period covered by this report. This is small when compared with the gamma radiation received from natural sources by populations throughout the world. Libby (*6*) estimates that the average external dose from natural sources, both terrestrial and cosmic, is of the order of 75 millirads per year, or 300 millirads in four years. On this basis, the gamma dose delivered from fallout is about 3 percent of the average gamma dose from natural sources. Thus, even the maximum theoretical dose from fallout to date is a small fraction added to the gamma dose received from natural radioactivity, and this slight increment is considerably smaller in magnitude than the normal variations in natural dose which occur from place to place throughout the world.

The significance of the deposition of strontium-90 in the quantities shown in the tables can be understood in relationship to the occurrence of natural radium, with which strontium shares many chemical properties. In the upper 1 foot of the earth's crust, radium is present in amounts approximating 1000 millicuries per square mile. This radium, like other trace elements, is absorbed into all living things. Adult North Americans contain about

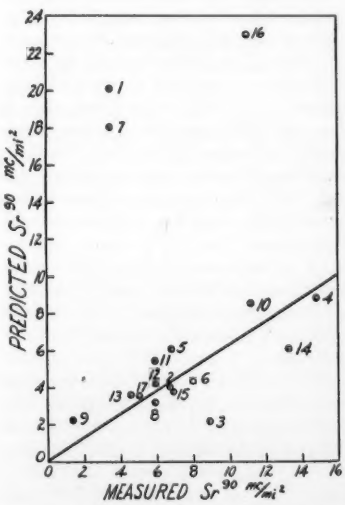

Fig. 2. Plot of measured versus predicted strontium-90 for soils from 17 locations in the United States: *1*, Albuquerque; *2*, Atlanta; *3*, Binghamton; *4*, Boise; *5*, Des Moines; *6*, Detroit; *7*, Grand Junction; *8*, Jacksonville; *9*, Los Angeles; *10*, Memphis; *11*, New Orleans; *12*, New York; *13*, Philadelphia; *14*, Rapid City; *15*, Rochester; *16*, Salt Lake City; *17*, Seattle.

10^{-4} microcuries of radium, which may be taken as the biological equilibrium of the radium burden of human beings in relation to the general environmental radium content of the upper 1 foot of soil. This amount (10^{-4} microcuries) is 1/1000 the maximum permissible radium burden of 0.1 microcurie and more nearly one 1/10000 the minimum amount that is known to have produced injury to human beings.

Natural radium and strontium-90 in fallout have differences in properties which may influence the ease with which they pass from soils into biological systems; therefore, one cannot conclude that, for any given soil content of strontium-90, the equilibrium human burden would be the same as the equilibrium body burden of radium at the same soil level. However, it is worth noting the minuteness of the present strontium-90 values in relation to the amount of radium present in all soils and, more particularly, in relation to the very much larger concentration of radium that could be safely tolerated.

A more direct method of evaluating the significance of the strontium-90 fallout is to measure the presence of this isotope, not only in soils, but in plants, animals, and human foodstuffs. Fortunately modern radiochemical techniques are sufficiently sensitive so that it is feasible to detect this isotope at concentrations comparable with that of radium and other naturally occurring isotopes. Measurements of this type have been undertaken and have succeeded in demonstrating the absorption of strontium-90 in foods. The concentration of this isotope, as expected, is dependent on the calcium content of the food, and for this reason the results can be expressed best as strontium-90 activity per gram of calcium. On this basis, milk in the United States during early 1956 contained about 3 micromicrocuries of strontium-90 per gram of calcium. One microcurie of strontium-90 (7) is the commonly accepted permissible content for the adult skeleton (8). The skeleton contains about 1000 grams calcium, and the permissible concentration would thus be 1000 micromicrocuries per gram of calcium, or about 350 times the presently observed concentration in milk.

According to the National Academy of Sciences (9), "Already some children have accumulated a measurable amount of radioactive strontium in their bodies. The amount, however, is quite small—a thousandth of what is considered a permissible dose."

References and Notes

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5. G. M. Dunning, *Sci. Monthly* **81**, 265 (1955).
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8. The permissible concentration of strontium-90 is probably lower by a factor of 10 than the concentration that would produce injury. On the other hand, the 1-microcurie level was established for occupational exposure, and the National Committee for Radiation Protection recommends that such levels be reduced to 10 percent for public exposure.
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E. C. Crittenden, Physical Standards Expert

Dr. Eugene C. Crittenden died in Washington, D.C., on 28 March 1956 at the age of 75. He had been a member of the American Association for the Advancement of Science for 40 years. Born at Oswago, Pennsylvania, 19 December 1880, he graduated from Cornell University in 1905 with a B.A. degree—not, as his many associates assumed, in physics—but rather in classical languages. He did, however, have a divided interest in physics and remained as a graduate student and instructor at Cornell University until he accepted an appointment at the National Bureau of Standards as an assistant physicist in July 1909.

Dr. Crittenden was first assigned to the photometric laboratory, where he subsequently made many important contributions. He was named chief of the bureau's electrical division in 1921 and continued in this position until 1946. Under his leadership, the program of the division expanded substantially, keeping pace with the rapid developments in radio and electronics. Major organizational units of the bureau developed from nuclei assembled under Dr. Crittenden's leadership. These include the former ordnance development division, now the diamond ordnance fuze laboratories of the Department of the Army, and the bureau's central radio propagation laboratories at Boulder, Colorado.

In 1933, Dr. Crittenden was made assistant director of the bureau. Subsequently, this title was changed to associate director. Until his retirement in 1950, he was the bureau's senior associate director and, in this period of changing administration and directors, was often called upon to serve as acting director of the bureau. For his outstanding contribution to the Government and to science, he was honored with many awards and recognitions.

For his outstanding contributions to the work of the bureau, Dr. Crittenden was awarded the Department of Commerce gold medal for exceptional service in 1949, which was the year that these awards were established. In 1946 he was honored with the gold medal of the Illuminating Engineering Society for "meritorious achievement conspicuously furthering the profession, art, or knowledge of illuminating engineering." Also in 1946, the Case Institute of Technology awarded him an honorary D.Sc. degree as "a devoted servant of the public, exponent of precise measurement, and international authority on the standards of science and industry."

Dr. Crittenden took an active part in American and international scientific societies. He was president of the Illuminating Engineering Society in 1925, president of the U.S. National Committee of the International Electrochemical Commission from 1939 to 1946, and president of the Optical Society of America in 1932–33. He served as an associate editor of the *Review of Scientific*

Instruments and as chairman of the editorial board of the National Bureau of Standards. He was chairman of the Interdepartmental Screw Thread Committee in 1952. He was very active in the standardization work of the American Society for Testing Materials; American Standards Association, in which he was chairman of the standards council; the International Organization for Standardization; and the American Institute of Electrical Engineers. The esteem of his associates is well indicated by his election to the presidency of the Cosmos Club of Washington.

Outstanding in Dr. Crittenden's achievements was his participation in the establishment of international standards in electricity and photometry and the writing of the Public Law 617 of the 81st Congress, passed on 21 July 1950, in which the Congress adopted these international standards as the nation's standards and then placed the standards and units of electricity and photometry on the same legal and commercial basis as our standards of mass, length, volume, and time.

As vice president of the International Commission on Illumination from 1939 to 1948 and president of its U.S. National Committee from 1928 to 1935, he played a major role in the establishment of modern photometric units, standards, and methods of measurement. These activities culminated in the international adoption of the "candela" in 1948. In recognition of his outstanding leadership in the field of illumination, he was elected an honorary life member of the International Commission on Illumination in 1950. As the United States representative on the International Committee on Weights and Measures from 1946 to 1954, and its vice chairman from 1950 to 1954, and as chief of the bureau's electrical division for many years, he was a leading scientific figure in replacing the obsolescent international system of electric units by the so-called absolute electric units.

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R. S. Breed, Bacterial Taxonomist

Dr. Robert Stanley Breed, whose death occurred 10 February 1956, distinguished himself in three fields of bacteriology, first in the dairy field, then in public health and sanitation, and finally in the nomenclature and classification of microorganisms. It is the last of the three fields to which he gave chief attention during the last decade of his life and for which he is likely to be longest remembered.

Born in 1877 at Brooklyn, Pennsylvania, he spent his college years at Amherst, from which he graduated in 1898 and then took an M.S. degree at the University of Colorado and a Ph.D. degree at Harvard in 1902. He began his professional career by teaching biology at Allegheny College, Meadville, Pennsylvania. His early training and teaching experience in general biology determined his approach to bacteriology. As a result, although his attention to the practical aspects of bacteriology in dairying and sanitation was great, the interest closest to his heart was taxonomy.

He was called to the New York State Agricultural Experiment Station at Geneva, New York, to take over the division of bacteriology that had been started by H. A. Harding a number of years previously. One of his first efforts in that division was to establish a general feeling for bacteriology as a science, bringing this about by calling frequent seminar meetings to discuss general bacteriological problems. He did not neglect the practical side, however. Before coming to Geneva, he had already established a reputation in sanitary milk inspection, because of his proposal to use the microscope as a quick method of counting bacteria in milk. It was natural, therefore, that his chief activities, during his first years at Geneva were in the dairy field. It was another logical development for him to turn to milk sanitation and related public-health fields. He served for many years, in the American Public Health Association, as chairman of the Committee on Standard Methods for Analysis of Dairy Products. At one period of his life, he was best known in this public-health field, and he remained active in it until the mid 1940's. During this same period, in addition to belonging to several nonprofessional organizations, he became especially active in the Society of American Bacteriologists and served as its president in 1927.

It was in the 1920's, during the period of his greatest activity in the bacteriological society, that he became especially interested in the *Manual of Determinative Bacteriology,* prepared by an earlier president of the society, D. H. Bergey of the University of Pennsylvania. Dr. Breed collaborated with Bergey in getting out the second, third, and fourth editions of the book and, after Bergey's death in 1937, became chief of a board of editors of three members, who took over the manual and developed it through two more editions, each larger and more complete than the preceding. He developed this manual into a cooperative undertaking in which some 100 collaborators were taking part. Although they all contributed, he was always the guiding spirit. A seventh edition was in preparation at the time of his death, and, although he left it far from finished, the remaining editors hope to complete the undertaking without too great delay.

As editor of this manual after Bergey's death, Breed contributed much to systematic bacteriology. In 1948 he retired from the experiment station and gave the remaining 8 years of his life to this undertaking. It was a labor of love with him, and he kept diligently at it until the day he died, even through a period of ill health about 1950 and a siege of eye trouble during his last 6 months. His ability to keep the numerous details of bacterial nomenclature in his head was astonishing to everyone who was associated with him.

Bacteriology has lost one of its outstanding members. Dr. Breed will be missed by many, especially by those who were associated with him in the activities of his last years.

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Society of the American Bacteriologists, Geneva, New York

News of Science

Insect Hosts of Plant Viruses

Most plant viruses are transmitted from plant to plant by insect vectors. Evidence has been accumulating for some years that in certain cases the insect may be more than a mechanical carrier of the virus; that is, the insect may serve as an alternative host for the virus. Certain plant viruses can be transmitted from one generation of insects to the next by transovarial passage without the need for an intermediate plant host. Others, such as the aster-yellows virus, are acquired naturally by the insect through feeding on a diseased plant. After feeding, the insect vector becomes infective for other plants only after an incubation period of about 10 days, but it then remains infective for the remainder of its life.

The aster-yellows virus can be transmitted in the laboratory from one leafhopper to another by mechanically injecting into normal insects the juice of ground-up virus-infected insects, as was demonstrated originally by L. M. Black in 1940. Later the virus was transmitted from insect to insect in indefinite series by injection while the insects were maintained on plants that did not support growth of the virus [Maramorosch, *Phytopathology* **42**, 59 (1952); for a review of the literature on multiplication of plant viruses in insect vectors see Maramorosch, *Advances in Virus Research* **3**, 221 (1955)]. The presence of virus in the insects is demonstrated by placing them on healthy aster plants and observing the plants for the symptoms of the yellows disease.

Cross-protection tests have long been used to determine whether or not two plant viruses are closely related. For instance, plants that are infected with California aster-yellows are resistant to eastern aster-yellows virus, and vice versa. Since both virus strains may be transmitted by the same species of leafhopper, it was possible to do a cross-protection test in the insect vector as well [Kunkel, *Advances in Virus Research* **3**, 251 (1955)]. Leafhoppers were infected with one of the two viruses by letting them feed on infected plants, and then two weeks later they were exposed to the second virus by the same technique. After a further incubation period, they were tested to see which virus they would transmit to susceptible plants. Invariably the insects were able to transmit only the virus to which they were first exposed. Thus, there is interference between these two virus strains in the insect host as well as in the plant host.

Although the aster-yellows virus multiplies in its insect vector, it causes no obvious disease symptoms, and the infected leafhoppers live as long and breed as freely as noninfected individuals. However, a careful cytological study of the tissues of infected and virus-free leafhoppers [Littau and Maramorosch, *Virology* **2**, 128 (1956)] revealed changes in the cells of the fat-body. In uninfected insects the nuclei of these cells were round, and the cytoplasm was homogeneous and heavily stained with azure B. In infected insects the nuclei of the fat-body cells were mostly star-shaped, and the cytoplasm was reticulate and less intensely stained with azure B. The authors suggest that these cytological changes are evidence of disease and that the aster-yellows virus may multiply in the cells of the fat-body.

Recent developments in tissue-culture techniques have suggested further experiments on the growth of aster-yellows virus in insects. Leafhoppers in the nymph stage were fed for 2 days on plants diseased with aster-yellows virus. If the insects were ground up at this time and the juices were injected into adult insects, no virus could be recovered and demonstrated by the infectivity of the injected insects for aster plants. If the nymphs were permitted to live for 10 days, the incubation period for infectivity of the virus, and then ground up, the virus was readily recovered by injection of the juice into adult insects. Some of the leafhopper nymphs after feeding for 2 days on diseased plants were anesthetized and cut up, and the pieces were incubated in tissue-culture fluid for 10 days. At this time it was possible to recover virus by injecting the juice of the ground-up tissue-culture fragments into adult leafhoppers [Maramorosch, *Virology* **2**, 369 (1956)]. This experiment indicates that the aster-yellows virus can develop infectivity in cultures of insect tissues, as well as in the living insect, and suggests that the culture of individual organs may demonstrate the actual site of virus infection in the leafhopper.—M. H. A.

New Technique for Machining Tungsten

At the North American Philips Laboratories, R. Levi, has developed a technique [*Philips Tech. Rev.* **17**, 97 (1955)] to machine tungsten, which otherwise as a solid is so brittle that any machining is practically impossible.

For this purpose tungsten powder is compressed at about 2000 kg/cm², is presintered at 1150°C, and then sintered some more at 2400°C in a water-free reducing atmosphere. The density of the ingots reaches the value of 83 to 84 percent of solid tungsten. This porous material is next infiltrated with a filler that does not alloy with the tungsten itself. Gold, copper, and alloys of the two in all proportions seem to be suitable for these requirements.

The ingot is placed on top of a weighted amount of copper, slightly in excess of the amount that would be necessary to fill all the pores, and is impregnated at a temperature of about 1350°C. Capillary action then fills all the pores, and this is facilitated by a hydrogen atmosphere and its fluxing action. The filler not only fills all the pores but acts as a lubricant during the machining operation.

When the machining is completed, the volatilization of the copper is effected by heating the machine parts in a vacuum furnace to 1800° to 1900°C for a sufficient time. Spectroscopic examination shows only extremely faint traces of copper. Intricate parts of different sizes, including very small ones, can, in this way, be made to close the dimensional tolerances.—K. L. H.

Timber Outlook

The U.S. Department of Agriculture has issued a nontechnical publication entitled *People and Timber*, which is based on the *Timber Resource Review*, a 3-year study made by the USDA's Forest Service with the collaboration of state foresters, state agencies, forest industries, and other private and public organizations.

The annual timber cut is 48.8 billion board feet. By the year 2000, timber needs are expected to rise to 80 to 100 billion board feet a year because of an expanding economy and an increased population. According to the study, these

increased needs can be met if all forest land is put under good management. About one-fourth of the forest land in this country is not growing nearly as much timber as would be possible under good management.

Insects, disease, and fire each year kill 13 billion board feet of sawtimber, an amount equal to one-fourth the net sawtimber growth. In addition they weaken big trees, delay natural restocking, and cause other serious losses in growth.

Of the timber cut, 25 percent is not used at all, the Forest Service study showed. Some residue will always be left in the woods and at the mills, but development of new uses for wood residues and improved methods of logging and sawing can reduce such losses.

According to the Forest Service, improved methods of forest management are most needed on the farm and other nonindustrial private timber holdings, most of them less than 100 acres in size.

The progress made in the last decade, the booklet points out, indicates what can be done. The growth of softwoods in the East now exceeds the cut of softwoods. Productivity is relatively good on forest industry and public lands. Gains are being made in forest-fire prevention and control. Wood is holding its own as an industrial material with consumption at an all-time high.

Korean Mineral Assay Laboratory

The Taejon Mineral Assay Laboratory, built and equipped by the United Nations Korean Reconstruction Agency (UNKRA) to help Korea utilize its mining resources to best advantage, has been formally turned over to the Ministry of Commerce and Industry of the Republic of Korea.

Since its official opening in March 1954 the laboratory, under the supervision of UNKRA technicians, has tested and examined Korea's mineral deposits and trained Korean mining graduates in various metallurgical processes. In the past year its capacities were extended to include facilities for mine owners and professors who wished to carry out individual research.

In making the formal transfer at a ceremony held at Taejon, John B. Coulter, agent general of UNKRA, described the activities of the laboratory and said, "Korea has many sources of mineral wealth, the full extent of which has yet to be measured. We know that gold, graphite, tungsten, lead, and copper deposits exist, which may aid in the industrial development of Korea and earn foreign exchange.

"To assist in the exploitation of these resources, the United Nations Korean Reconstruction Agency built this assay laboratory at Taejon and installed the most modern equipment for conducting mineral analyses and metallurgical tests.

"The laboratory has now been operating for over 2 years, often analyzing more than 300 samples a month, to determine the commercial value of existing mines and to evaluate new deposits. It is fully manned with a trained Korean staff, and is already meeting the essential needs in this field. It is the best equipped laboratory of its kind in the Far East."

Acetoglyceride Process Patented

A basic patent on the preparation of the chemically modified fats known as acetoglycerides has just been granted and is now available for licensing without cost. The patent was granted to Reuben O. Feuge, Earl J. Vicknair, and Klare S. Markley, as a result of work done at the Southern Utilization Research Branch of the Agricultural Research Service, U.S. Department of Agriculture. It is U.S. Patent No. 2,745,749, "Glyceridic mixtures exhibiting unique properties and process for their production"; copies may be purchased for 25 cents each from the U.S. Patent Office, Washington, D.C.

Investigations leading to issuance of the patent were concerned with cottonseed, soybean, peanut, and other vegetable oils. It was found that acetylation of monoglyceride mixtures of these oils with fatty acids containing two to four carbon atoms yielded products with a number of unique and desirable properties. Some of these products are flexible, waxlike, and nongreasy in texture and appear to have many possibilities for use in the food industry, such as coatings for meat products, cheese, candies, ice-cream bars, and other foods. Melting points of acetoglycerides can be varied for special requirements, and some of the products hold the desired texture over a relatively wide range of temperatures. Another advantage of the acetoglycerides is their resistance to oxidation, or rancidity. Aside from food and cosmetic uses, they also have possibilities as plasticizers, lubricants, and the like.

Peabody Museum Expedition

The Peabody Museum of Salem, Mass., is the sponsor of an expedition to the South Seas by the yacht *Varua*, captained by William Robinson. Robinson is accompanied by the photographer, Eliot Eliosofohn, and the entomologist, David Bonnet.

During a lengthy cruise among the Pacific islands, the expedition will attempt to trace the origins of the Polynesian people and solve a problem that has interested scientists and laymen alike since the first Pacific explorations of Captain Cook in 1768. Interest on the part of the general public has been stimulated lately by the voyage of Thor Heyerdahl and his assistants on the balsa raft *Kon Tiki* in these waters.

A new approach will be used in an endeavor to determine the possible origin of the Polynesians. Recent findings of entomologists and research workers indicate that a particular type of filaria, apparently confined to people of the Polynesian race, is distributed throughout the archipelago and also extends across the Pacific to the mainland of southeast Asia.

The route that the expedition will follow was planned at the museum by Donald S. Marshall, research anthropologist for Polynesia, and Ernest S. Dodge, director, in consultation with Bonnet. During a 6-months' cruise, stops will be made at each of a series of selected islands, where information about the natives, as well as blood samples for filaria, will be gathered.

Messages by Meteor Trails

A Canadian Defence Research Board team has developed a new communications technique that uses the trials of single meteors to transmit messages over long distances. Called "Janet" on its inception 4 years ago, the project's principles have just been declassified by the Canadian Department of National Defence.

P. A. Forsyth, of the Radio Physics Laboratory at Shirley Bay near Ottawa, first visualized the practical possibilities of using individual meteor trails from the ionosphere as a communications aid. Hundreds of meteors enter the earth's atmosphere every hour. They leave behind, at a height of about 60 miles, trails of charged particles that can reflect radio waves. Forsyth and his associates discovered that these trails can be used for communicating between distant points on the earth's surface. Experiments have proved that the signals can be transmitted by the "Janet" method for distances up to 1000 miles.

Although large meteors occasionally flash through the atmosphere, those used in the "Janet" system are tiny particles about the size of a pinhead, which leave a trail of electrons. The equipment required for the transmission of messages by this new technique is relatively simple. Because the method is reliable and uses low-power equipment, efficient and economical long-range communication systems for all-season use are a possibility.

The system employs frequencies previously used only for short-distance transmission, such as television broadcasts. Because these frequencies are considerably less crowded than those now being

used for long-distance communication, this in effect opens a new band for long-distance use.

The equipment at each of the two widely separated ground stations employs many of the recently developed computer, or "electronic brain," techniques. When the circuit detects a suitably located meteor trail in the upper atmosphere, the message previously stored at one station is transmitted automatically and rapidly to the other end of the circuit.

Because each meteor can be used only for about a second, transmission must take place in short bursts at very high speeds. The actual transmission speed is much too high to be received by standard teletype equipment. The incoming information, therefore, is held in storage and printed at normal speeds during the intervals between transmission bursts.

This high-speed "burst" transmission technique and the frequent presence of meteors in the upper atmosphere permit the passage of lengthy messages between stations in a relatively short time.

Because the signals reflected from the trails are largely independent of ionospheric conditions, such as disturbances caused by the aurora borealis, meteor trail transmissions will be particularly valuable for Canada with its vast distances in the aurora belt.

Tranquilizing Drugs and Behavioral Disorders

The behavioral disorders that commonly afflict mentally retarded children —ranging from destructiveness and breath holding to psychogenic vomiting and teeth grinding—have responded in many cases to treatment with tranquilizing drugs, particularly chlorpromazine ("Thorazine") and meprobamate ("Miltown"), according to a report in the June issue of the *International Record of Medicine and G. P. Clinics,* by I. N. Kugelmass, consultant to the Departmet of Health and Hospitals, New York City. The degree of relief varied with the type of disorder, but the two drugs were of value in from 40 to 80 percent of the cases in most disorders.

Meprobamate appeared to be more effective in relieving teeth grinding, nail biting, head banging, tics, phobias, anxiety, destructiveness, and sleeplessness. Chlorpromazine proved more helpful in relief from vomiting and abnormal appetite, restlessness, lip sucking, hyperactivity, anger, cruelty and aggression, negativism, sleepwalking, and night terrors.

Kugelmass emphasized that the drugs are not cures, that they "merely suppress the overt manifestations without eliminating the underlying pathology."

The study involved 250 mentally retarded children, treated individually and in institutions over a 5-year period. Ten drugs in all were evaluated for their effectiveness in treating 25 spearate symptoms, but only chlorpromazine and meprobamate were effective in relieving most of the symptoms.

Irrigation and Power in Australia

According to the National Geographic Society, a major irrigation project is under way in New South Wales, Australia. The Snowy River, which drains the Snowy Mountains of the Australian Alps and flows south to empty into the South Atlantic at a rate of 0.5 million gallons per minute, will be diverted through the mountains by means of a network of dams, tunnels, and canals, so that it will feed into the Murray and Murrumbidgee rivers, which flow through the arid plain northwest of the Snowy Mountains. The latter rivers are already being used to the maximum for irrigation. When the project is completed, it will consist of seven major dams, ten smaller dams, 85 miles of mountain tunnels, and 400 miles of canals.

It is expected that the entire construction project will require about 20 years, The system, when completed, will provide annually some 2,333,000 acre-feet of water for irrigation and about 3 million kilowatts of electricity for power. The latter will be developed by 17 power stations, some of which will be fed by water passing through penstocks that will pass vertically through as much as 1000 feet of rock.

Scientists on TV

Scientists from Harvard University and Massachusetts Institute of Technology will take part in a filmed series of 23 television programs designed to introduce viewers to the scope and methods of physics, chemistry, astronomy, and geology. The films are for national distribution to educational TV stations.

The series has been organized by Philippe LeCorbeiller, professor of general education and of applied physics at Harvard University. It will be produced by the Lowell Institute Cooperative Broadcasting Council in the studios of WGBH-TV, channel 2, Boston, under contract with the Educational Television and Radio Center, Ann Arbor, Mich.

Each program will focus on a single idea essential to an understanding of modern scientific thinking. The presentation will include experimental demonstrations and graphic illustrations. Some of the topics will be: "Science and common sense"; "The size and age of the universe"; "Are atoms real?" "How science grows"; "Nature and the laboratory"; and "The role of scientific imagination."

"My objective in giving this series on TV," LeCorbeiller points out, "will be to try to bridge the gap between the scientists and the public. It is out of the question to inform everybody about the endless intricacies of laboratory science. It is all the more important to find some way of making the American public a partner in the never-ending conquest of the unknown. The ideal way for that is television."

LeCorbeiller will be joined in the presentation of the programs by Gerald Holton, Leonard K. Nash, I. Bernard Cohen, Bart J. Bok, Harlow Shapley, Kirtley F. Mather, all of Harvard, and Sanborn C. Brown of Massachusetts Institute of Technology.

Laboratory for Gulf Fisheries

Problems related to finding, catching, and processing Gulf of Mexico fish and shellfish will be studied at the new fishery laboratory that is to be constructed this year at Pascagoula, Miss., for the U.S. Fish and Wildlife Service. The contract for the construction of the new laboratory and auxiliary buildings has been awarded to the Oden Construction Company of Hattiesburg, Miss., for $165,000. Engineers of the service's regional office in Atlanta, Ga., will exercise general supervision of construction.

Research on methods and techniques for providing the highest quality pack of shrimp, oysters, tuna, and other South Atlantic and Gulf seafoods will be one of the main tasks of the new laboratory. Heretofore technologic work for the Gulf and South Atlantic areas was handled through the service's laboratory at College Park, Md.

The new installation will provide facilities for the exploratory fishing and gear development program that is already being conducted in the Gulf area. The service's exploratory fishing vessel *Oregon,* which operates in the Gulf of Mexico, is based at Pascagoula in connection with this program.

Irregular Milking Schedule

According to a report to the *New York Times,* studies carried out during a period of 2 years at the Ruakura Animal Research Station in New Zealand show that carefully matched herds of cows produce as much milk and butterfat per day when they are milked at 16- and 8-hour intervals (at 8 A.M. and 4 P.M.) as when they are milked at the

traditional 12-hour intervals (at 5 A.M. and 5 P.M. in New Zealand).

If this finding should be accepted by dairy farmers, their working hours could be greatly modified. Similarly, work shifts in dairy factories, which manufacture butter and cheese, would be markedly changed.

Medical Reactor

The U.S. Atomic Energy Commission has recently awarded a contract for the construction of the first nuclear reactor designed specifically for medical research housed in a new medical center at Brookhaven National Laboratory. The center will include laboratories for medical physics, pathology, microbiology, biochemistry, and physiology as well as a 48-bed research hospital. The medical center, including the reactor, is scheduled for completion in 1958 at a cost of $6 million.

Employing thermal neutrons, the new medical reactor will produce a treatment beam having an intensity 50 times greater than that provided by the Brookhaven general research reactor and, thus, will insure wider medical application of neutrons and flexibility of treatment.

Fossil Palm

Roland W. Brown, paleontologist of the U.S. Geological Survey and the Smithsonian Institution, has recently discovered fossil imprints of palmlike leaves in a geologic formation in southwestern Colorado, which dates from the Triassic period. He has assigned the species tentatively to the palm family and described it as a hitherto unknown genus, *Sanmiguella,* of the great plant group of Monocotyledons, which includes palms, grasses, sedges, and many other flowering plants.

The fossils of the area where the fossils were discovered presumably accumulated on flood plains and in scattered pools and lakes at a time when the southwestern Colorado area was a few hundred feet above sea level. Plant remains are rare.

Teeth of ancient reptiles, the phytosars, which were somewhat similar to extant crocodiles although they belonged to a different family, were associated with the palmleaf imprints.

News Briefs

■ A bill that would have authorized Federal construction and operation of nuclear reactors for the production of electric power was recently returned to the Joint Atomic Energy Committee by a vote of 203 to 191 in the House of Representatives. In effect, this killed the bill, which had already passed the Senate.

■ Fabrication has begun on the nuclear research reactor designed and being built by Atomics International, a division of North American Aviation, Inc., for the Atomic Energy Research Institute of Japan. The 50-kilowatt reactor will use as fuel enriched uranyl sulphate dissolved in about 4 gallons of water and will be similar to the industrial research reactor designed and built by Atomics International for the Armour Research Foundation in Chicago, which began operating recently.

The reactor for Japan is designed to prevent the discharge of any radioactive gases or other fission products into the atmosphere. The gases will be retained inside the primary system, where they will be circulated and recombined. This will have the added advantage of providing a source of neutron-free gamma rays, which are essential in medical and scientific research.

The Atomic Energy Research Institute in Japan, a nonprofit foundation sponsored by the Japanese government and industry, will use the reactor for nuclear study—including medical research, drug sterilization, food preservation, production of radioisotopes, and research and study in reactor techniques—as well as for investigating the effects of atomic radiation on plastics, rubber, and similar materials, and for research in botany, biology, and agriculture.

■ An experimental seeding of quinoa, a hardy plant whose seeds and leaves have long been eaten by the upland natives of Peru, Bolivia, and Ecuador, will be undertaken in Greenland under the auspices of the U.S. Navy, according to a report from the National Geographic Society. If the seeding is successful, Greenland will have a staple food plant. On the altiplano of Peru and Bolivia, quinoa is a major food plant, which grows well at altitudes up to 13,000 feet.

Scientists in the News

HUGH R. GILMORE, JR., colonel in the Medical Corps, U.S. Army, and curator of the Medical Museum of the Armed Forces Institute of Pathology, has retired. He has been cited by Silas B. Hays, Surgeon General, U.S. Army, for 30 years of superior and devoted service to the Army Medical Service. His appointment to the Medical Museum post in 1953 climaxed a long association with military medicine. He received his M.D. in 1921 from the University of Pennsylvania and, after several years in private practice, joined the Army Medical Corps in 1926.

Gilmore is a former chief of pathology and allied sciences division of the Army Surgeon General's Office and has served in many capacities at medical installations, both in the United States and overseas. Throughout World War II, he was assigned as preventive medicine officer to various command headquarters in the North African and Italian theaters of operations. Gilmore served as acting curator of the Medical Museum for 9 months during a previous tour of duty at AFIP from 1935 to 1937.

SAMUEL W. KIME, captain, Medical Corps, U.S. Army, has been named acting curator of the Medical Museum.

MARVIN L. ENGLISH, who has been teaching engineering at North Carolina State College, will become associate professor of mechanical engineering in the University of Cincinnati College of Engineering on 1 Sept. 1956.

EARL H. DEARBORN has been appointed head of pharmacological research at Lederle Laboratories, American Cyanamid Company. He was formerly professor of pharmacology and chairman of the department at the Boston University School of Medicine.

JOHN H. GARLOCK, clinical professor of surgery at Columbia University and director of surgery at Mount Sinai Hospital, New York City, is at present on an extended teaching tour of South America. He is scheduled to give a series of lectures and hold didactic operative clinics in every important medical center. His itinerary includes Colombia, Chile, Peru, Argentina, and Brazil.

THEODORE EUGENE STERNE has left the staff of the U.S. Army's Ballistic Research Laboratories at Aberdeen, Md., and has been appointed to concurrent positions as associate director of the Astrophysical Observatory of the Smithsonian Institution in Cambridge, Mass., and as Simon Newcomb professor of astrophysics in Harvard University. At Aberdeen, Sterne's work was in the fields of exterior ballistics, terminal ballistics, wound ballistics, and weapon systems evaluation.

He was connected with Harvard University from 1931 to 1941, first as a National Research fellow in physics at Harvard and M.I.T., and then as a lecturer in astrophysics.

L. WHITTINGTON GORHAM has been made director emeritus and GEORGE K. HIRST has become acting director of the Public Health Research Institute of the City of New York, Inc.

Recent appointments to the staff of the National Bureau of Standards are as follows. WILLIAM S. CONNOR will work in the statistical engineering section of the applied mathematics division on the application of modern probability and statistical methods to the physical sciences. He was previously employed at NBS from 1951 to 1954.

JULIAN F. SMITH will extend the present scope of the instrumentation reference service of the office of basic instrumentation. Prior to his appointment, he spent 4 years as a documentation and technical information service consultant, largely at the Library of Congress.

FRANK A. GRANT, who formerly was an assistant professor of physics at the University of Maryland, will do research in the mineral products division on the semiconducting properties of titanium dioxide and titanates.

At the cryogenic engineering laboratory of the Boulder laboratories of the bureau, ROBERT B. JACOBS has been appointed chief of the cryogenic equipment section, replacing BASCOM W. BIRMINGHAM who has been made chief of the cryogenic processes section.

WILLIAM D. GRAY has been named head of experimental pharmacology in the research division, American Cyanamid Company, at Lederle Laboratories, Pearl River, New York. He was formerly group leader in pharmacological research.

G. ARTHUR COOPER has been appointed head curator of the U.S. National Museum's department of geology. He will continue to serve as curator of invertebrate paleontology and paleobotany, a position he has held since 1943.

JOHN A. CLARK, a member of the Massachusetts Institute of Technology faculty since 1949, has been appointed professor of mechanical engineering at the University of Michigan and will start with the second semester of 1956–57.

JOHN J. DENTON has been named director of organic chemical research at the Pearl River laboratories of the American Cynamid Company. He was formerly technical director of Cyanamid's fine chemicals division.

Two Netherlands visiting professors have been announced by the University of Michigan. J. DROOGLEEVER FORTUYN, professor of neurology at the University of Groningen, will join the department of anatomy of the University of Michigan Medical School from January to June 1957; and M. G. RUTTEN, professor of physical geology at the University of Utrecht, will serve in the department of geology, College of Literature, Science and the Arts, for the 1957–58 university year.

JOSE DEL CASTILLO, professor of biophysics at University College, London, England, has been appointed visiting professor of physiology at the State University College of Medicine in Brooklyn for 1 year beginning 1 Sept.

J. C. HACKLEMAN, University of Illinois professor of crops extension, will retire from the university staff on 1 Sept., to join the staff of the Illinois Crop Improvement Association as its public relations officer.

WILLIAM F. MANN, JR., will be the new head of the Southern Forest Experiment Station's research center at Alexandria, La. He succeeds JOHN T. CASSADY, who will take charge of the East Gulfcoast Research Center in western Florida and southern Alabama.

RANDOLPH T. MAJOR, former scientific vice president of Merck and Company and more recently in an advisory capacity at Merck, has been appointed professor of chemistry at the University of Virginia.

Recent Deaths

ELMER C. BERTOLET, SR., Philadelphia, Pa.; 68; director of chemical laboratories at the Research Institute of Temple University; 16 July.

CHARLES W. BONNEY, Germantown, Pa.; 82; professor and surgeon on the staff of Jefferson Medical College; 21 July.

A. NOWELL CREADICK, Durham, N.C.; 73; clinical professor emeritus of obstetrics and gynecology at Yale University Medical School; 23 July.

JOHN P. DERINGER, Los Angeles, Calif.; 53; metallurgist; 20 July.

CARL R. ENGLUND, Fullerton, Calif.; 71; expert on radiotelephony; retired member of the staff of Bell Telephone Laboratories; 22 July.

RICHARD W. FESSENDEN, Amherst, Mass.; 54; professor of chemistry at the University of Massachusetts; 23 July.

MALCOLM GOODRIDGE, New York, N.Y.; 83; former professor of clinical medicine at Cornell University Medical College; 23 July.

ARTHUR D. HOLMES, Amherst, Mass.; 71; professor emeritus of chemistry at the University of Massachusetts; 18 July.

ELIHU KATZ, New York, N.Y.; 68; professor of gastroenterology of the New York Polyclinic Hospital; 20 July.

PIERRE J. RABIL, Washington, D.C.; 43; assistant professor in surgery at Georgetown University Medical Center; 23 July.

ALEXANDER RICE, Newport, R.I.; 80; founder of the Institute of Geographical Exploration and professor emeritus of geographic exploration at Harvard University; 23 July.

FRANCIS B. TRUDEAU, SR., Saranac Lake, N.Y.; 69; authority on tuberculosis; 20 July.

MANFRED WAHL, Germantown, Pa.; retired microbiologist; 7 July.

LIGHTNER WITMER, Devon, Pa.; 89; founder of the psychological clinic at the University of Pennsylvania and its director for 35 years; former member of the faculty at Bryn Mawr College and Lehigh University; 19 July.

Education

■ A program for advanced training of psychiatrists in New York State's mental hygiene institutions will be started in September. The program will be under the joint direction of the State University of New York and the New York State Department of Mental Hygiene. In its initial phase, it will provide training for medical staffs of six mental hygiene institutions in the metropolitan area in cooperation with the faculty of the State University Medical School at Brooklyn. A similar program also is planned for staffs of mental hospitals upstate. This will be centered around the State University's Medical School at Syracuse.

■ A new graduate program in nautical engineering, leading to the degree of master of science, will be started in September by the Stevens Institute of Technology. The new program, with classes to be held in the evening, is designed to help ship designers fulfill present-day demands for vessels that will travel at high speeds in rough, as well as smooth, seas. The staff, consisting of members of the regular Stevens faculty and the group at the institute's Experimental Towing Tank Laboratory, will teach recently developed techniques in fluid dynamics, statistical methods, dynamical structural analysis, and model testing.

■ The science consultant program of the University of Texas, which was established by a grant from the AAAS has added two consultants to its field staff. They are Alan Humphreys, formerly a science teacher at Belton High School, and John Wagner, formerly a mathematics teacher at Kerrville High School. Humphreys and Wagner, together with Wayne Taylor, who is executive direc-

tor of the new program and Extension Teaching and Field Service Bureau associate professor, will visit high schools within 200 miles of Austin to confer individually with teachers on methods of improving laboratory instruction, sources, and use of materials. They will also aid in organizing science clubs, fairs, and other programs designed to encourage science students. Finally, they will participate in in-service training programs for teachers and address professional meetings.

Grants, Fellowships, and Awards

■ The American Heart Association has awarded grants-in-aid totaling $1,042,817 to 180 scientists engaged in research in this country and in three foreign countries in the field of cardiovascular diseases. These funds come from contributions by the public to the Heart Fund campaign conducted each February.

Almost every known field of biological investigation is represented in the list of projects. Many fall into the category of basic research, with a number of investigations concerned with tracing the metabolic pathways of heart muscle. The grants also provide for an intensive inquiry into the nature of atherosclerosis, including studies of substances found in the blood which under normal conditions appear to "clear" it of fats after a heavy meal, and of the effects of hormones on the fat content of the blood.

In addition, there are studies of enzymes that may serve as the body's mechanism for breaking up blood clots, studies of the use of anticlotting drugs in the long-term treatment of coronary artery disease, studies of the circulation and functioning of the kidney, and studies of the influence of the nervous system in setting up a chronic constriction of the smallest arteries. A number of investigations are in the field of rheumatic fever, and some of them will seek to explain why a streptococcal infection leads to rheumatic fever in some individuals but not in others. Further, some projects are seeking to improve existing surgical procedures and to develop new ones, procedures, for example, for operating on the heart in a "dry field" using heart-lung machines or lowered body temperatures. Experimental studies in blood vessel grafts to replace diseased arteries are also receiving support.

■ The American Dermatological Association is again offering a series of awards for the best essays submitted for original work, not previously published, relative to some fundamental aspect of dermatology or syphilology. The cash awards will range from $500 to $200. Essays will be judged on the basis of originality of ideas, potential importance of work, experimental methods and use of controls, evaluation of results, and clarity of presentation. For information write to J. Lamar Callaway, Secretary, American Dermatological Association, Duke Hospital, Durham, N.C.

■ Nine grants, totaling $367,182, to conduct research and demonstrations in the field of hospital service and administration have been announced by the U.S. Public Health Service. Aimed at finding ways to improve the care of patients in hospitals and health facilities, reduce costs, and help make the benefits of hospital and health services more widely available, this research is part of the Hospital Survey and Construction (Hill-Burton) Program.

■ The Rockefeller Foundation has awarded a grant of $105,000 to the Boyce Thompson Institute for Plant Research to be spent over a 5-year period. The money will be used to support the work of Lawrence P. Miller, Robert G. Owens, and S. E. A. McCallan on mechanisms of fungicide action. The investigation will include the use of radioisotopes to study the uptake and metabolism of fungicides by fungus spores and host plants, determination of the effect of fungicides on enzyme systems in spores, and studies on the nature of the fungicidal action of sulfur.

■ A $300,000 program of research concerned with preserving the human resources of the state of Michigan has been initiated at the University of Michigan. The program is financed by an appropriation from the state legislature and will cover a 12-month period. Fourteen projects have been undertaken by various schools and colleges of the university.

■ The National Foundation for Infantile Paralysis has made grants totaling $1,952,155.05 to 27 institutions for scientific research in the fields of virology and epidemiology, prevention and treatment of aftereffects of polio, and support of poliomyelitis respirator centers.

The awards reflect efforts by the National Foundation to rescue polio patients with paralyzed respiratory systems from dependence on mechanical breathing devices. Eight of the current grants are to polio respiratory centers supported by the National Foundation. The program, begun in 1950, has attracted world-wide medical attention and now encompasses 15 treatment-research centers.

The foundation has also made 19 grants totaling $1,211,983 to aid teaching programs bearing on the treatment of poliomyelitis patients.

Miscellaneous

■ Opportunities for research in a number of fields bearing on the use of southern farm crops are now being offered at the Southern Research Branch, New Orleans, of the Agricultural Research Service, U.S. Department of Agriculture. Openings range from a starting salary of $8990 per year for mature scientists to $3175 per year for scientific aides. The positions are graded under federal Civil Service in accordance with training and experience. Chemists specializing in organic, physical, or analytic chemistry or biochemistry are needed; also needed are physicists, cotton technologists, chemical and textile engineers, and mechanical engineers to help develop cotton-processing machinery. Application should be made through the U.S. Civil Service Commission, Eighth Civil Service Region, 1114 Commerce St., Dallas, Tex. For information write to C. H. Fisher, Chief of the Southern Utilization Research Branch, 1100 Robert E. Lee Blvd., New Orleans 19, La.

■ As a tribute to the memory of an outstanding physician, teacher, and investigator, the associates and friends of John Punnett Peters are seeking funds to create a resident lectureship or visiting professorship in his name. The lectureship would be offered periodically to outstanding scientists in all areas of medicine from any part of the world.

For information write to Paul H. Lavietes, Secretary, John Punnett Peters Memorial Fund, Yale University School of Medicine, New Haven 11, Conn.

■ A program to keep blind people informed of the progress of science has been initiated by T. A. Benham, assistant professor of physics at Haverford College, who has been blind since the age of 2 years. Books in scientific fields and a monthly magazine, *Science Recorded,* will be made available as tape recordings. The recordings of books will be accompanied by a supplement in Braille, which will contain explanatory material in the form of mathematical equations, graphs, tables, and a summary of the spellings of scientific words.

■ University of Michigan botanists will begin work this fall on the state's first complete, up-to-date handbook on local flora in more than 50 years. The cost of the undertaking will be an estimated $60,000.

The principal investigator for the project will be Edward G. Voss, of 1015 Lincoln Ave., Ann Arbor. Much of his work will be centered in the university herbarium, which contains about 300,000 specimens of flowering plants.

Reports

Possible Mechanism of Tolerance to Narcotic Drugs

Although many hypotheses have been offered to explain the development of tolerance to narcotic drugs (*1*), adequate experimental data have not been presented to elucidate this phenomenon. In recent studies at this laboratory, we have observed several striking similarities between the receptors for narcotic drugs and the enzymes that N-demethylate these drugs. The enzymes and receptors have been found to be alike with respect to substrates with which they interact, stereospecificity, and antagonism by N-allylnormorphine (*2*). Since the enzymes that N-demethylate narcotic drugs were similar in several ways to narcotic drug receptors, it appeared likely that these enzymes might serve as a model for the receptors. Thus, any changes occurring in enzyme activity during the development of tolerance might reflect changes taking place on the drug receptor. With this in mind, an examination of the effect of repeated administration of morphine to rats on the enzymic N-demethylation of morphine and other narcotic drugs was undertaken. The effect of the administration of morphine, together with its antagonist, N-allylnormorphine, on enzymic N-demethylation was also investigated, since it has been shown that this combination reduces the development of tolerance (*3*).

Twelve rats were made tolerant to morphine by a daily intraperitoneal injection of morphine sulfate. The animals were given an initial dose of 20 mg/kg of morphine sulfate, and the amount of drug administered was then progressively increased during a period of 35 days until daily injection of 150 mg/kg was reached (group M). Another group of eight rats was given N-allylnormorphine and morphine in a ratio of 1/4 for 35 days (group NM). A group of 12 rats was given the same dosage regimen of morphine as described in group M for 35 days, following which the drug was abruptly withdrawn for 12 days (group W). Fourteen rats receiving a daily injection of isotonic saline served as controls (group C). Fisher-strain male rats that were 120 to 130 days old when the study was begun were used throughout the study. The average gain in weight in all groups of rats was approximately the same.

Twenty-four hours after the test period the animals were sacrificed, and the livers were examined for their ability to N-demethylate morphine, dilaudid, meperidine (Demerol), and cocaine. The livers were prepared for enzyme assay by a procedure described previously (*2*), and the degree of enzymic N-demethylation was determined by estimating the amount of formaldehyde liberated (*4*).

The changes in the enzymic N-demethylation in the various groups of rats are shown in Fig. 1. In the case of morphine-treated animals (group M), a profound reduction in the ability to N-demethylate morphine occurred. In addition, the enzymic N-demethylation of dilaudid, a compound that shows cross-tolerance to morphine (*5*), was reduced to about the same degree as that of morphine, while the demethylation of meperidine, a drug that exhibits limited cross-tolerance to morphine (*6*), was only partially reduced. Enzymic N-demethylation of cocaine, for which no cross-tolerance to morphine occurs (*5*), was unaffected by chronic morphine administration. In the group of animals that was treated with both N-allylnormorphine and morphine (group NM), the reduction in the enzymic demethylation of narcotic drugs was significantly less than in those that received morphine only. The enzyme activity with respect to all substrates had returned to the control level or above in withdrawn animals (group W).

Other pathways in the *in vitro* metabolism of narcotic drugs, such as O-demethylation of codeine (*7*), hydrolysis of diacetyl morphine (*8*), and conjugation of morphine (*9*), were also examined. No differences in the enzymic O-demethylation, hydrolysis, and conjugation of narcotic drugs in the control- and morphine-treated rats were found.

From the results described here, a striking parallelism between the enzymic N-demethylation of narcotic drugs and the development of tolerance to these drugs was found. The repeated administration of morphine reduced both enzymic demethylation and pharmacological response. In addition, there was a correlation between demethylation of substrates and cross-tolerance to morphine. Furthermore, N-allylnormorphine, which blocks development of tolerance to morphine, also blocks reduction of enzyme activity. It appears that N-allylnormorphine not only antagonizes the pharmacological action and the enzymic demethylation of narcotic drugs but also protects the enzyme and perhaps the receptor sites. Animals that are withdrawn from narcotic drugs recover their pharmacological responses to these drugs; similarly, the demethylating-enzyme activity in rats withdrawn from morphine returns to normal.

The changes in enzyme activity in morphine-treated rats suggest a mechanism for the development of tolerance, if one assumes that enzymes which N-demethylate narcotic drugs and the receptors for these drugs are probably closely related. The continuous interaction of narcotic drugs with the demethylating enzymes inactivates the enzymes. Likewise, the

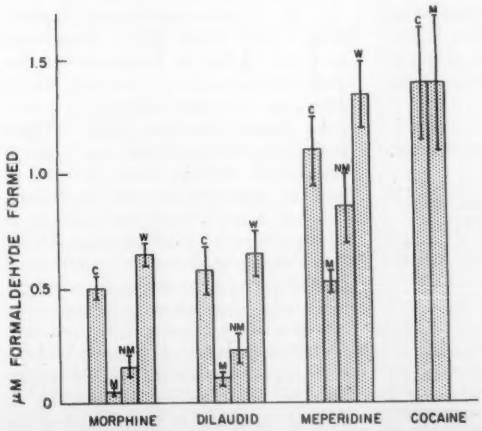

Fig. 1. Effect of morphine treatment, N-allylnormorphine, and withdrawal on the enzymic N-demethylation of narcotic drugs. Vertical bracketed lines on bars are standard deviation of the mean. (group M) morphine-treated rats; (group NM) morphine- and N-allylnormorphine-treated rats; (group W) rats treated with morphine and then withdrawn; (group C) normal rats.

continuous interaction of narcotic drugs with their receptors may inactivate the receptors. Thus, a decreased response to the narcotic drugs may develop as a result of unavailability of receptor sites (*10*).

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4 June 1956

Apomorphine Test for Tranquilizing Drugs: Effect of Dibenamine

When a minimal emetic dose of apomorphine is carefully established in a group of dogs, it is possible to detect the inhibiting effect on emesis of a second drug, such as diphenhydramine (*1*), chlorpromazine (*2*), or reserpine (*3*). These findings indicate that the apomorphine test may have utility in selecting tranquilizing agents and imply a link between central emetic mechanisms and activities effecting tranquil behavior.

The rationale for the apomorphine test lies in the drug's established site of action at the chemoreceptor trigger zone in the area postrema, an area afferent to the emetic center which lies more deeply in the lateral reticular formation of the medulla. This center may be excited reflexly from the periphery, through the chemoreceptor trigger area or from rostral neural sites (*4*). It is adjacent to areas integrating and mediating vasomotor, respiratory, and postural responses and functionally related to adjacent and rostral brain-stem areas involved in extrapyramidal, visceral, and "alerting" functions. The emetic integrating mechanisms are thus linked with a complex of brain-stem operations that bring the individual physiologically into contact with both his internal and external environment. This complex of operations may mediate the change in level and quality of psychomotor and autonomic reactivity which characterizes tranquil behavior. The link between emetic mechanisms and tranquilization is thus a neural one.

Table 1. Proportion of dogs protected from emesis by dibenamine.*

Time to emetic challenge	Apomorphine dose (μg/kg)	
	2 × M.E.D. (60)	4 × M.E.D. (100)
20 min	0/4	0/4
2½ to 6 hr	3/3	3/6
24 hr	7/7	2/3

* In acid alcohol solution (0.4 percent), at a dose of 2 mg/kg intraperitoneally; apomorphine minimal emetic dose (M.E.D.) established at 25 μg/kg.

Apomorphine has central effects other than an emetic action. These apomorphine actions implicate the adjacent neural systems—for example, a hypotonic effect on spasticity produced either by decerebration or anterior cerebellar section (*5*) and, in the human, with subemetic doses, a tranquilizing action (*6*). It is entirely possible that drugs inhibiting the action of apomorphine at the chemotrigger area do so in part by action on these adjacent systems, which in turn may affect the reactivity of the emetic center.

One cannot use tests of emetic reactivity indiscriminately to infer tranquilizing or antiemetic clinical utility. Reserpine, for example, antagonizes apomorphine emesis in the dog but in the pigeon and in man may produce nausea and vomiting (*7*). Interpreting apomorphine tests, one may infer a brain-stem site of action; this is indicated by positive results and not at all ruled out by negative findings.

This report describes a centrally mediated antiapomorphine effect of dibenamine. A powerful adrenergic blocking agent, the drug acts peripherally on the effector cell to block chiefly the excitatory effects of epinephrine. Nickerson (*8*) has cited two phases in dibenamine activity: an initial epinephrine-dibenamine antagonism for the first 2 hours, and, with the binding of dibenamine to the peripheral effector cell, the onset of true adrenergic blockade enduring for 3 or 4 days. During the first phase, a brief period of central excitation may be noted, presumably affecting temporal lobe, as well as hypothalamic and medullary, function. Since a hydrolysis product of dibenamine which lacks adrenergic blocking properties produces the central effects of the first phase, the initial central effects may not be attributed to alteration of central adrenergic systems. Since no central effects had been experimentally demonstrable for the second phase, the finding of a prolonged tranquilizing action in anxiety states had to be ascribed to the peripheral blockade of adrenergic substances related to tension states (*9*), and the finding that catatonic patients were brought tranquilly into contact for a period of 18 to 72 hours was attributed to a possible action on central blood vessels (*10*). It would therefore be important to demonstrate an alteration of central neural activity that would be coincident with the behavioral effects and the peripheral adrenergic blockade of the second phase. Results of dibenamine inhibition of apomorphine emesis are indicated in Table 1.

With chlorpromazine and diphenhydramine, antiemetic potency is apparent during the peak period of pharmacologic activity (*1, 2*). With dibenamine, however, antiemetic potency is not demonstrable during the first 2 hours after administration. Following this initial period, and for a period up to 24 hours (the longest interval tested), a definite inhibition of apomorphine-induced emesis has been observed. The prolonged action thus establishes a central neural basis for the noted behavioral effects. This action is related neither to the adrenergic blockade (sympathectomy does not alter apomorphine emesis) nor to a clinical antiemetic effect. Both the excitatory phase and the local gastric irritation can produce nausea or vomiting.

The demonstration of prolonged central neuronal alteration does raise the possibility that less toxic agents with greater tranquilizing potency may be found among some of the interesting chemical analogs of dibenamine (*8*). From the experimental viewpoint, several clues point to particular receptor systems altered by dibenamine (*6, 8, 11*), so that the drug may now prove useful as a tool to study central drug-enzyme systems.

The fact that a drug may induce long-enduring central changes the neural bases for which are masked, stresses the importance in neuropharmacology of searching for such latent actions. In this respect, the apomorphine test of medullary vomiting mechanisms may be but one of several possibilities for studying brain-stem reactivity in attempting to develop drugs that affect psychic function.

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31 May 1956

Self-Stimulation of the Brain Used as a Screening Method for Tranquilizing Drugs

Behavioral effects of reserpine and chlorpromazine in animals and man have led to the search for an adequate screening method that would relate both to behavior in animals and site of action in the brain. Such a screening method is described here on the basis of the finding (*1*) that electric stimulation applied to specific hypothalamic and paleocortical structures of the rat brain has an effect on behavior tantamount to primary reward.

In these experiments (*2*), a bipolar electrode was chronically implanted in the brain of each animal. The pair stimulates only at the tip, and thus it affects only a small area of the brain. For testing, the animal was placed in a lever box (Skinner box), and an electric circuit was set up so that each bar-press produced a train of electric stimulation 0.6 sec in duration through the implanted electrode. The stimulus used was a 60-cy/sec sine wave of from 1 to 1.5 v applied through a resistance of about 10,000 ohms. In tests, the animal was never stimulated by the experimenter but was allowed to stimulate itself by pressing the lever.

The reinforcing value of an electrode placement is assessed in terms of the frequency of the lever-pressing response. When electrodes are placed in the anterior or middle hypothalamus, extremely high response rates can be achieved, often rising above 5000 responses per hour. When electrodes are placed in the region of the septal area or the amygdaloid complex, rates range from 200 to 2000 per hour. Rates of 200 responses per hour are also achieved from all structures of the rhinencephalic cortex. Other parts of the brain do not produce this positive reinforcing effect.

The size and anatomical differentiation of this "rewarding" system suggested that its parts might be differentially sensitive to neuropharmacological agents. Experiments were therefore designed to determine whether different agents would affect self-stimulation rates for some electrode loci more than for others.

In the series reported here, electrodes were implanted in the middle hypothalamus, the septal region of the forebrain, or the amygdaloid area. Each animal had an electrode pair in only one of these regions. Animals were allowed 4 days to recover from the operation and then were given 6 to 14 days of pretraining at self-stimulation in the test boxes. In training and tests, the animals were run for 80 minutes per day. The electric stimulus was the only reinforcing agent used in these experiments. Under these conditions, all animals showed day-to-day improvement during pretraining and achieved stable response prior to drug tests. The stable response rate of animals that were stimulated in the septal region of the forebrain or the amygdaloid area was about 500 per hour, and the stable response rate of animals that were stimulated in the middle hypothalamus was about 2500 per hour.

After stable rates had been achieved, drugs were introduced on the basis of a modified Latin square with crossing over of drugs between animals and control runs on intervening days to measure carry-over effects.

The preliminary series reported here consisted of a limited range of doses of reserpine, chlorpromazine, and pentobarbital. The effectiveness of a given dose was gauged by evaluating the response rate following drug administration as a percentage of the average response rate for all days when no drug was administered.

In three animals with electrodes placed ventromedially in the hypothalamus, reserpine at 1 mg/kg depressed response rates to 7 to 45 percent of normal. In two rats with electrodes implanted in the amygdala, the same dose of reserpine reduced the response rates to 1 and 22 percent of normal. In contrast, the response rates of four rats in which the electrodes were placed in the septal region of the forebrain were depressed to a mean of 75 percent of normal (range, 67 to 83 percent.) Thus, there was marked depression in rats that were stimulated in the hypothalamus or in the amygdala but only a minor depression produced in the rats that were stimulated in the septal region. Typical data are presented in Fig. 1.

Chlorpromazine (2.5 mg/kg) depressed response rates in rats that were

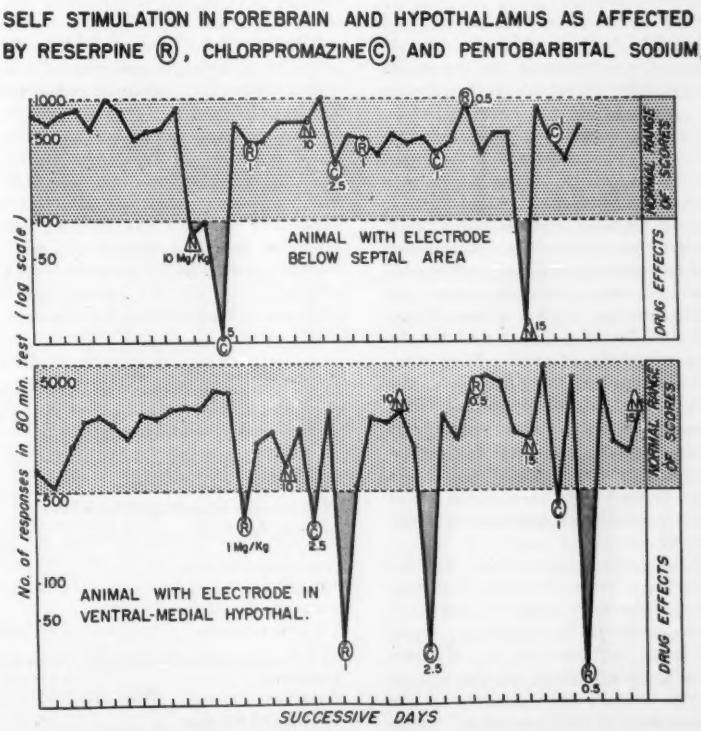

Fig. 1. The number of responses in 80-minute test periods plotted for each day of the experiment for two representative rats. The top graph presents data for a typical rat with an electrode implanted in the region below the septal area. Reserpine at 1 mg/kg and 0.5 mg/kg and chlorpromazine at 2.5 mg/kg and 1 mg/kg produce no major change in response rate; pentobarbital at 10 mg/kg slightly depresses responding on first, but not on second, administration. The lower graph presents data for a typical rat with an electrode placed in the posterior ventromedial hypothalamus. Doses of reserpine (1 mg/kg) and chlorpromazine (2.5 mg/kg) produce sharp falls in response rates; pentobarbital has little effect. Both rats were responding for a 1 v, 60 cy/sec sine wave stimulus.

stimulated in the hypothalamus to 0 to 11 percent of normal (Fig. 1). The response rates of two rats stimulated in the amygdala were depressed to 1 and 17 percent of normal. With the same dose, the response rates of six rats stimulated in the septum were depressed to a mean of 38 percent of normal (range, 0 to 77 percent). Three of the animals had scores of 50 percent or higher following administration of the drug. Thus, chlorpromazine appears to have selective effects similar to those of reserpine, but the effects are more variable.

Smaller doses of reserpine and chlorpromazine depressed the response rates of rats stimulated in the hypothalamus but rarely altered response rates in rats stimulated in the septal region.

Pentobarbital at doses of 10 mg/kg did not have similar selective depressant effects, although one aberrant animal showed a depressant effect. At doses of 15 mg/kg, marked motor depression made it difficult to assess the data; animals stimulated in the hypothalamus, however, have been seen to give high response rates even with this extreme dose.

Increasing sensitivity to reserpine on successive administrations at 1 or 0.5 mg/kg was also found in these experiments. This is illustrated in Fig. 1 by the greater depression caused by the second 1-mg and the second 0.5-mg dose for the rat stimulated in the hypothalamus.

From these preliminary studies it appears that, in the rat, the rate of self-stimulation through electrodes implanted deep in the brain may be used as a behavioral screening method to distinguish tranquilizing agents from other central nervous system depressants, and possibly also from each other. Reserpine and chlorpromazine, at doses without observable side effects, have been shown to depress selectively at certain brain sites, thus distinguishing them from pentobarbital, which has no selective effects. At doses of the tranquilizing agents large enough to produce gross changes in spontaneous motor activity, selectivity between animals stimulated in the septal region and the hypothalamus is no longer observed.

These observations are being extended by the use of other electrode placements and a wider dose range of these and other agents. Such techniques should lend insight into selective sites of action of tranquilizing agents. Studies now in progress relating primary drives to the various parts of the "rewarding" system may provide a basis for interpreting the differential drug effects.

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Heat Denaturation of Serum Albumin in Presence of Perfluorooctanoic Acid

Based on studies of the interaction between bovine serum albumin (BSA) and perfluorooctanoic acid (PF) ($C_7F_{15}COOH$) (*1*) and the initial observation that PF may prevent the heat coagulation of BSA (*2*) similar to the studies of Ballou *et al.* (*3*), an investigation was undertaken of the physical-chemical and immunochemical properties of BSA-PF complexes heated under controlled conditions (*4*).

Solutions of 0.33-percent BSA in the presence of varying amounts of PF in acetate buffers of 0.1-ionic strength at *p*H 5.44 or 5.72 were autoclaved at 105°C and 15-lb pressure in thin-walled, sealed, 10-ml ampoules for 20, 30, 40, 50, 60, and 120 minutes, respectively. The solutions were stored in a refrigerator for 1 week, after which it was observed that only those systems composed of a minimum of 266 moles of PF per mole of BSA remained clear. For the immunochemical reactions with calibrated rabbit anti-BSA sera, the various solutions were adjusted to *p*H 7 to 7.5 without appreciable change in protein concentration.

Sedimentation patterns were obtained at two rotor speeds—namely, 42,040 and 56,100 rev/min. Typical sedimentation constants, corrected for adiabatic expansion of the rotor, are assembeld in Table 1. From the variation of the sedimentation constants as a function of the gravitational field and of heating time, it may be concluded that heated BSA and PF form complexes of micellar nature. Because many types of micelles could exist —each with its own critical micelle concentration—one would expect that the area under each sedimenting peak would decrease with increasing sedimentation time and with change of concentration across the boundary. These area losses are different from those observed by Brand (*5*), inasmuch as they cannot be accounted for by the sedimentation of large aggregates at low speeds, and inasmuch as they become more pronounced as heating time is increased.

The reversibility of PF binding in heated samples was investigated by exhaustively dialyzing these solutions against 20 volumes of buffer and following their behavior at periodic intervals, both in the ultracentrifuge and by immunochemical analysis. The ultracentrifugation study (Table 1) indicated that micelles still remained, for area losses were observed in all dialyzed heated solutions. The *p*H of the dialyzates was raised to 7.4 in order to utilize electrostatic repulsion to dissociate complexes, but even this procedure did not reduce area losses, nor did we observe a component the sedimentation of which was equal to that of native BSA at the same concentration. When the *p*H of the dialyzates was low-

Table 1. Sedimentation constants of BSA-PF complexes. Area losses were observed in autoclaved samples. The numbers in parentheses represent average relative proportions (percentage) of total schlieren areas.

Experimental conditions	Sedimentation constants, $S_{20,w}$							
*p*H 5.44, mole ratio PF to BSA = 293/1								
Unheated, 56,100 rev/min	14.50	(84.3)	17.81	(15.7)				
Autoclaved 20 min, 56,100 rev/min	15.58	(37.5)	27.79	(50.0)	82.5	(12.5)		
Autoclaved 20 min, 42,040 rev/min	16.46	(36.6)	23.78	(63.4)				
*p*H 5.72, mole ratio = 468/1, 56,100 rev/min								
Unheated	10.47	(32.5)	13.95	(67.5)				
Autoclaved 30 min	7.35	(9.0)	10.98	(50.4)	14.74	(32.3)	20.82	(8.3)
Autoclaved 60 min	10.69	(57.6)	14.64	(42.4)				
*p*H 5.72, mole ratio = 366/1, 56,100 rev/min								
Autoclaved 120 min	11.13	(39.2)	15.14	(45.9)	18.95	(14.9)		
Autoclaved 120 min, dialyzed 3 times, *p*H 5.72	5.76	(44.4)	14.60	(55.6)				
Autoclaved 120 min, dialyzed 5 times, *p*H 7.41	4.55	(67.2)	10.72	(32.8)				
BSA control	4.05	(100)						

Table 2. Immunochemical reaction of autoclaved BSA-PF complexes, with rabbit anti-BSA serum.

*p*H at heating time	mole ratio	heating time (min)	Denaturation (%)
5.72	366/1	120	100
5.72	293/1	20	73
5.44	293/1	20	73
* 5.72	293/1	20	87
† 5.44	293/1	20	67

* Dialyzed five times against *p*H 7.5 buffer.
† Dialyzed against buffer of *p*H 4.9, precipitate removed, supernatant redialyzed against buffer of pH 7.5.

ered to 5.2, a sizable precipitate appeared. This property, as well as the general appearance of the exhaustively dialyzed solutions in the ultracentrifuge, resembled observations reported on heat-denatured BSA (*6*).

The aggregation phenomenon in unheated samples is strikingly different from that in autoclaved ones. No physical-chemical or immunochemical evidence of denaturation is observed provided that heating is eliminated. Even in the presence of large amounts of PF, where aggregation is very pronounced, the following properties of BSA remain unchanged: partial specific volume at 25.0 ± 0.03°C at 0.734, intrinsic viscosity at 0.0414. Under the same conditions, the partial specific volume of PF was 0.401 and its intrinsic viscosity 0.0108. This might indicate that the over-all hydrodynamic shape of the unheated aggregates is not markedly different from that of the native BSA molecule.

A mechanism of BSA-PF complex formation at low temperatures was previously proposed (*7*) by postulating that the fluorine atoms interact with protein hydrogen bonds. This interaction could be reversible as long as the water layer surrounding the protein remains essentially undisturbed. At high temperatures, where the configuration is known to be disrupted, it is conceivable that PF molecules could penetrate the water layer, form some "direct" hydrogen bonds, and thus solubilize the denatured protein near its isoelectric point (*p*H 5.2). Exhaustive dialysis at that *p*H, however, precipitates the heat-denatured protein.

Immunochemical studies with BSA-PF complexes corroborated the physical-chemical findings that PF does not protect BSA from heat denaturation. Although quantitative immunochemical techniques were employed in these studies, the results obtained can only be interpreted qualitatively. Results obtained in the region of antibody excess through the equivalence zone indicated that significant changes had occurred in BSA. The figures in the last column of Table 2 refer to the amount of the protein relative to native BSA which did not precipitate with anti-BSA. This does not imply that the heated complex that did precipitate with anti-BSA was completely unaltered, as shown by the following. (i) If the BSA-PF complexes are not fractionated by differential dialysis, the maximum amount of total nitrogen could never be precipitated. (ii) Even after dialysis at *p*H 5.6 and 4.9, which led to the removal of appreciable amounts of insoluble (denatured) material, the soluble protein did not react like native BSA. In some cases its behavior resembled that of an aggregated molecule as evidenced by a broad equivalence zone.

From the results presented here (*8*) it would appear that BSA cannot be protected against heat denaturation at 175°C. Furthermore, from viscosity and partial specific volume studies alone, no deduction can be made concerning the interaction of unheated BSA-PF complexes. A serious discrepancy therefore exists between our findings and results previously published (*9*).

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18 May 1956

On Respiratory Impairment in Cancer Cells

Some years ago Otto Warburg (*1*) enunciated a theory of cancer which, briefly summarized, proposed that cancer originates when a nonneoplastic cell adopts an anaerobic metabolism as a means of survival after injury to its respiratory system. According to Warburg, the tumor is initiated by a damaged respiration, which persists as a characteristic feature of the neoplastic condition. In a recent paper, entitled "On the origin of cancer cells," originally published in German (*2*) and then translated into English (*3*), Warburg reiterates this hypothesis and claims further support for it on the basis of experiments with ascites tumor cells. I recognize the great debt that biochemists owe this illustrious investigator and regret the necessity of taking issue with his basic biochemical premise, namely, that cancer cells have an impaired respiration.

In a comprehensive review of this subject in 1939, Burk (*4*) first pointed out the essentially fallacious reasoning behind this hypothesis. More recently, Schmidt (*5*) and I (*6*) reviewed this topic independently in the light of modern findings and concluded similarly that there is no sound experimental basis for the belief that oxidative metabolism in tumors is impaired. It is recognized by all, including Warburg, that despite their high glycolysis, oxygen consumption is not quantitatively diminished; by and large, a representative group of tumors absorb oxygen about as rapidly as a comparable group of nonneoplastic tissues (see, for example, Burk's extensive tables, *4*). An early statement by Warburg, illustrative of his views concerning the relationship between the high aerobic and anaerobic glycolysis of tumor cells and their oxygen consumption, is the following (*1*, pp. 139–141).

"We determined the Meyerhof quotient for carcinoma tissue, lactic acid bacteria, embryonic tissue and a number of other glycolyzing tissues, and as a rule obtained the same mean values as Meyerhof. As a rule 1 mol. of breathed oxygen, just as in muscle, causes the disappearance of 1–2 mol. lactic acid. This result . . . proves that the influence of the respiration on the cleavage metabolism in the carcinoma-cell is normal. . . . Although in the tumor every oxygen molecule breathed is just as effective as in muscle—the Meyerhof quotient is equal in the two cases—yet the respiration does not cause the glycolysis to disappear. The respiration of the carcinoma tissue is too small in comparison with its glycolytic power."

Thus, according to Warburg, the Meyerhof quotient (a quantitative expression of the Pasteur effect) is normal in carcinoma, and oxygen consumption is also not quantitatively diminished; but respiration is disturbed, because glycolysis persists in oxygen. As I pointed out earlier (*6*, p. 276), I believe it would be more accurate to state that anaerobic glycolysis is so high in tumors that a normal respiration and a normal Pasteur effect are incapable of eliminating it.

Although Warburg still states categori-

cally that ". . . the respiration of all cancer cells is damaged. . . ." (*3*, p. 309), he has given no clearer justification now for this view than he did 26 years ago. In Table 1 (*3*), he shows that whereas liver, kidney, and embryo have Q_{O_2}'s of -15, the ascites tumor has a Q_{O_2} of -7. On these grounds he concludes that the tumor cannot utilize sufficient oxygen for its needs and thus requires fermentative energy. On the assumption that each mole of lactic acid formed from glucose yields 1 mole of ATP, and each mole of oxygen consumed gives rise to 7 moles of ATP, he calculates that the tumor obtains more than half of its potential phosphate bond energy by glycolysis, whereas the three noncancer tissues obtain theirs mainly by respiration. Accepting these results at their face value, it is still necessary to ask why some normal tissues manage to survive without glycolysis with Q_{O_2}'s of -3 to -6; also, why some tumors glycolyze highly with Q_{O_2}'s as high as -10 to -20 (*4*, pp. 438–441)? It is also pertinent to ask why certain nonneoplastic tissues, with moderate to high oxygen uptakes—for example, brain, retina, kidney medulla, and intestinal mucosa—glycolyze as highly as many tumors (*7*)? It is evident that all tumors produce large amounts of lactic acid, but so do many noncancer tissues; and just as noncancer tissues display a wide diversity in oxygen uptake, so do tumors.

Although it is unintentional, I am sure, Table 1 (*3*) gives misleading impressions that the respiratory and glycolytic activities are constant and characteristic for a single tissue, and that all tissues produce essentially the same amounts of phosphate bond energy. Actually, tissue even from a single organ will vary considerably in Q_{O_2} from one animal to another. In our experience, rat liver slices display Q_{O_2}'s ranging from -6 to -12 (usually about -7), and rat kidney cortex from -15 to -25. Biochemists are confronted with a wide variety of tissues of the most diverse respiratory behavior. Our present state of knowledge does not allow any categorical statements about what represents a proper respiratory activity for maintenance of either a normal or a cancer cell; nor can we state what is an optimal enzyme activity for a particular cell function.

Perhaps the most damaging evidence against the Warburg hypothesis has been obtained in isotope tracer studies (*6*, pp. 303 ff). The results of such studies leave no doubt of the ability of miscellaneous tumors to convert glucose (and fatty acids) to carbon dioxide at rates similar in magnitude to that of nonneoplastic tissues (*5*, *6*). It is difficult to imagine a type of respiratory disturbance not involving either a diminution in oxygen consumption or a loss in the ability to convert glucose and fatty acids to CO_2.

Warburg suggests in the present paper that perhaps the respiratory impairment may involve an inability to couple oxidation with phosphorylation. Here again, the available evidence does not support such a concept. Effects of inhibitors such as fluoride ion or dinitrophenol are similar in neoplastic and nonneoplastic tissues (*8*) and data of other investigators (*6*, p. 321) have given no indication that oxidative phosphorylation occurs in tumor mitochondria in a manner different from that in their noncancerous counterparts.

Another pertinent illustraton of the inadequacy of the Warburg concept is that it fails to consider that a large part of the respiration of cancer cells may be due to fatty acid oxidation. Although it seems fairly certain now that animal tissues generally, including the neoplastic, use fatty acids as a metabolic fuel, nowhere in Warburg's writings is there any consideration of the possible role played by fatty acids in the respiration of cells.

Another weakness of the Warburg hypothesis is that it does not fit in with what we have learned in recent years of chemical mechanisms of glycolysis and respiration. Again, Warburg states, "We need to know no more of respiration and fermentation here than that they are energy-producing reactions. . . ." (*3*, p. 309). This attitude may have been justified 25 years ago when little was known of their chemical nature. At present we recognize that they are not "independent metabolic processes" but are intimately related. To assume that respiration and glycolysis are separately activated, alternate means of cellular energy production, it is indeed necessary to ignore all that has been learned of their chemical mechanisms.

According to our present conceptions, the major pathway of oxidation of glucose to carbon dioxide in most animal cells, whether normal or neoplastic, involves its conversion to pyruvic acid by way of the Embden-Meyerhof process, oxidative decarboxylation of pyruvic acid to acetyl coenzyme A, and condensation of the latter with oxaloacetic acid to enter the citric acid cycle. Down to the pyruvic acid stage, respiration and fermentation follow a common pathway. The extent to which pyruvic acid, a common intermediary in both respiration and glycolysis, competes for electrons held by the pyridine nucleotides with those factors that transport electrons to oxygen—namely, the flavoproteins and cytochromes—should be a crucial factor in determining the degree of aerobic glycolysis.

If there is a disturbance in respiration that leads to an accumulation of lactic acid, it can occur only at or beyond the pyruvic acid stage and must be due either to some aberration in carbon transport through the citric acid cycle or to some "bottleneck" in electron transport. Many enzymatic and isotope tracer studies have fully established that the citric acid cycle operates in tumors (*6*, pp. 311 ff). Although cytochromes are reportedly low in tumors (*9*, pp. 404 ff), as are also some of the B vitamins involved in electron transport (*9*, p. 408), the generally unimpaired oxygen consumption already referred to clearly indicates that electrons reach oxygen about as readily in tumors as in other tissues. Thus, the available evidence indicates to me that high glycolysis occurs, *despite* quantitatively and qualitatively normal occurrence of carbon and electron transport. This can mean only that glucose catabolism is so rapid in tumors that the normal channels for disposal of pyruvic acid are overloaded. Many possibilities exist for explaining this high glucose catabolism, which do not involve disturbances in respiration. My colleagues and I are now attempting to unravel the multiplicity of factors concerned with lactic acid production in the intact cell.

I do not wish to minimize the significance of the high aerobic and anaerobic glycolysis of tumor tissue. It is conceivable that glycolytic activity, though not resulting from a faulty respiration, may play a special role in the neoplastic process. Data are available from the field of lipid metabolism, for example, which suggest that some phase of glucose catabolism in liver is coupled with fatty acid synthesis (*10*). The close association of lactic acid production with the neoplastic process, and with growth in general, makes this phenomenon a worthy subject of study.

Warburg states (*3*, p. 309), "We now understand the chemical mechanism of respiration and fermentation almost completely. . . ." We have, indeed, learned a great deal of what can happen in cells, and much of this can be credited to Warburg, who has played a large part in expanding our biochemical frontiers. The fact that progress has been so great in the past must make us aware, however, that future progress will also be great, and that our present knowledge is still primitive. Certainly we have much to learn before we can feel we understand the mechanisms that underlie the utilization of metabolic fuels for functional activities of cells.

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15 March 1956

In 1950 George Klein of the Karolinska Institute, Stockholm, was kind enough to send to Dahlem a strain of mouse ascites cancer that consists of nearly 100 percent cancer cells, that can be transplanted with 100 percent takes, and that is resistant to the shaking necessary in manometry.

Only since that time have we been able to determine quantitatively the metabolism of pure cancer cells. All our previous experiments (*1*) had been carried out with solid tumors—that is, with various mixtures of cancer cells and normal cells. The more cancer cells a tumor contained, the higher was the fermentation and the lower was the respiration. But no absolute values could be obtained.

Thus, the year 1950 brought about the transition from the study of the metabolism of the mixed cells to the study of the metabolism of pure cancer cells, a very great progress in cancer research (*2*). Weinhouse (*3*) is not appreciative of this progress, or of many important discoveries made since 1925—for example, the nonfermentation of the rapidly regenerating liver; the structural difference between energy production by respiration and by fermentation; the genetic autonomy of the respiring grana and the role of grana in the pathology of neoplasms; and carcinogenesis by respiratory poisons. Most of the comment by Weinhouse might have been written before 1925.

As expected, the fermentation of the pure cancer cells was found to be much higher than any previously observed fermentation of cancer cell mixtures. Indeed, mouse ascites cancer cells produced anaerobically per hour nearly 30 percent of their dry weight of lactic acid. In comparison with this enormous fermentation, respiration of the pure cancer cells was, as expected, very low.

Even more important were the results obtained in 1956 with Earle's *in vitro* cultures of pure mouse cancer cells. Such cells were available as two strains of high and low "malignancy," both derived from one and the same single cell. When, in the laboratory of Dean Burk, the respiration and the fermentation of these two strains of different malignancy but the same genetic origin were measured, the result was as follows: the higher the malignancy, the greater the fermentation and the smaller the respiration (*2*, pp. 313–314). The absolute fermentation values for the high-malignancy cells were as high as the values for the mouse ascites cancer cells.

These experiments with pure cancer cells—the ascites cells and Earle's cells of different malignancy—were decisive and conclusive. They correspond, in the problem of relativity, to the observed red displacement in the gravitational field.

Among normal cells, the nearest equivalent to pure cancer cells is the chorion in the first days of embryonic development. The chorion grows rapidly. It is histologically almost pure. It is so thin that it is not necessary to slice it for measurements of metabolism. It is so hardy that it can be shaken many hours in manometric vessels without disintegration. Anaerobically it produces 15 percent of its dry weight of lactic acid per hour, but aerobically it produces no lactic acid at all. Its respiration, in contrast to that of cancer cells, is high—indeed, nearly three times higher than the respiration of highly malignant, pure cancer cells.

Unlike the chorion, the whole embryo itself is unsuitable for such *in vitro* experiments, because it is disintegrated by the motion of the vessels if it is immersed in salt solutions or even in homologous serum. Yet the important question of lactic acid production by the living embryo can easily be decided by lactic acid determinations in the affluent and effluent blood vessels of an embryo *in situ* in a pregnant animal. If an embryo produced as much lactic acid as cancer cells, a very great increase in the effluent vessels would be found. But no increase has been found.

By these experiments—with chorion *in vitro*, and with the total embryo *in vivo* —it has been shown that intact embryonic cells, in contrast to cancer cells, produce no lactic acid aerobically.

Table 1. Average metabolic values obtained in serum with pure cancer cells of mice and with pure embryonic cells of mice. Q_{O_2} means cubic millimeters of oxygen consumed, and $Q_M{}^{O_2}$ and $Q_M{}^{N_2}$ mean cubic millimeters of lactic acid produced aerobically and anaerobically, respectively, per milligram (dry weight), per hour.

Cells	Q_{O_2}	$Q_M{}^{O_2}$	$Q_M{}^{N_2}$
Ascites cancer cells	−7	30	70
Earle's cancer cells (high malignancy)	−7	30	70
Earle's cancer cells (low malignancy)	−13	10	25
Chorion of young embryos	−17	0	35

Table 1 summarizes the average metabolic values obtained in serum with pure cancer cells of mice and with pure embryonic cells of mice. They constitute the main basic facts. $Q_M{}^{N_2} = 70$ means that the high-malignancy cancer cells produce anaerobically per hour an amount of lactic acid equal to 29 percent of their dry weight. The respiration, if normal, should be $Q_{O_2} = -35$, whereas $Q_{O_2} = -7$ was found. This means that the respiration of the high-malignancy cancer cells is only one-fifth of that of normal growing cells with $Q_M{}^{N_2} = 70$, and only two-fifths of that of growing chorion of young embryo with a $Q_M{}^{N_2} = 35$.

Obviously, nothing could be less enlightened than the opinion of Weinhouse that the respiration of cancer cells is as high, or even higher, than the respiration of normal growing cells. "High" and "low" respiration have greatest significance, of course, when compared with fermentation, as has been defined and emphasized many times since 1923, not only by the early use of such specific quotients as $Q_M{}^{O_2}/Q_{O_2}$, and $Q_M{}^{N_2}/Q_{O_2}$, but in my words of 1924 cited by Weinhouse, "The respiration of the carcinoma tissue is too small in comparison with its glycolytic power." Without such specification, "high" and "low" can become meaningless; thus, the absolute value of respiration of normal connective tissue is very low, and yet it is no cancer, because the fermentation too is very low.

Many years before the respiratory enzymes and the fermentation enzymes of oxidation-reduction were discovered at Dahlem, we reached the conclusion that the biochemical mechanism of fermentation and respiration in cancer cells is qualitatively the same as in normal cells, the differences being only quantitative, the one process being increased and the other decreased. Although later investigators have confirmed this general conclusion, Weinhouse takes exception to the phraseology "damaged respiration" of cancer cells. But because the facts are so clear and well defined, our abridged expression should not be objectionable. We have here a perfect example of a dispute about words.

It is something deeper when Weinhouse dislikes the statement that the shifting of the energy production from the aerobic to the anaerobic state is the cause of cancer. He feels that this is far too simple: How can cancer, as mysterious as life itself, be explained by such a simple physicochemical principle?

Yet this feeling is not justified. The problem of cancer is not to explain life, but to discover the differences between cancer cells and normal growing cells. Fortunately this can be done without

knowing what life really is. Imagine two engines, the one being driven by complete and the other by incomplete combustion of coal. A man who knows nothing at all about engines, their structure, and their purpose, may discover the difference. He may, for example, smell it.

OTTO WARBURG

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2 July 1956

A mass of experimental data published during the past 33 years has established the phenomenon of a metabolism characteristic of living cancer cells, including high anaerobic and aerobic glycolysis (formation of lactic acid from glucose) and an impaired respiration (*1, 2*). The impaired respiration may involve any combination—usually at least three—of the following experimental quantities readily measurable under appropriate conditions: (i) a high ratio of glycolysis to respiration; (ii) a low absolute value for oxygen consumption (Q_{O_2}); (iii) an inefficient or uncoupled respiration; or (iv) a low paraphenylenediamine (succinate) oxidative response (*3*). This list could be expanded.

Respiratory impairment in living cancer cells, first discovered by Otto Warburg in 1923, is an experimental fact, and not, as described by Weinhouse (*4, 5*) a hypothesis based on "essentially fallacious reasoning." Statements of Weinhouse indicating that the author of "Burk's extensive tables" has at any time ever denied the factual existence of an impaired respiration in cancer cells are categorically untrue.

The overwhelming evidence for the occurrence of various forms of respiratory impairment in neoplastic cells, available in some 1000 experimental papers, but denied by Weinhouse, obviously cannot be recapitulated in this note. It is, however, possible to outline here decisive errors in the most tangible support offered by Weinhouse for his central, underlying view that "by and large, a representative group of tumors absorb oxygen about as rapidly as a comparable group of nonneoplastic tissues . . . . oxygen consumption is not quantitatively diminished" (*6*). Curiously, this long-discarded but now exhumed view, which specifically denies a low Q_{O_2} in most cancer cells (impairment ii), is alleged to derive its main support from "Burk's extensive tables" (*7*). Weinhouse (*4*, p. 271) has selectively condensed parts of these extensive tables, on some incompletely defined basis, and arrived at the following average tissue slice Q_{O_2} values for three groups of tissues, each of which has a wide spread of individual values: 15 types of malignant tumors, −11.8; seven growing tissues (three types), −9.7; 14 nongrowing tissue types, −9.3. In short, by these statistics, the tumors would *appear* to have an average ("by and large") respiration that is not lower, but even higher, than that of either the growing or nongrowing tissues selected as "comparable."

But such average Q_{O_2} values are meaningless as they stand, both statistically and otherwise. They have not been adjusted for important species differences among the three groups, for medium effects, for cellular impurity in the tumors (normal tissues, ordinarily being 100 percent nonneoplastic, need no such adjustment), for differences of technique among the different investigators cited, and so forth. A remarkable error is Weinhouse's inclusion, in the already small group of growing tissues, of certain tissues that had first been severely predamaged by treatment with cyanide and anaerobiosis (!), thus lowering notably the calculated average Q_{O_2} for this group.

Weinhouse's statistical approach to the problem of possible Q_{O_2} impairment in cancer cells requires the use of the foregoing adjustments just as surely as cancer mortality and morbidity statistics require adjustment, in the absence of complete and perfect data. The types of adjustments listed all tend, without exception, to raise the Q_{O_2} values of normal tissues relative to tumor tissues, with the end result that, as one approaches truly physiological comparisons, one obtains average Q_{O_2} values for normal growing and nongrowing tissues that are "by and large" two to three times higher than those for tumors, with reduction in spread of individual values.

The first two types of adjustment listed are probably the most important quantitatively and will be briefly discussed by way of illustration. It is well established from the data extensively summarized and formalized, for example, by Krebs (*8*) and Adolph (*9*), that tissue respiratory rate, basal heat production, ventilation rate, and a host of other vital properties are marked, linear log-log functions of species body weight. The group of normal tissues selected by Weinhouse were from the rat, rabbit, dog, and man, but none from mice; the tumor tissue types selected were preponderantly from mice, the normal tissues of which have average rates of respiration and basal heat production far above those of the larger species, the basal heat productions being of the rough relative order 160, 100, 60, 35, and 25 in mice, rat, rabbit, dog, and man, respectively. Any reasonable (but imperative!) adjustment of average respiratory rate for species difference alone would place the tumor group well below that of the normal group, with an adjusted average Q_{O_2} value of −6 to −7 (instead of −11.8, (*10*). This value agrees with the grand average value that one obtains directly from all 30 widely varying types of malignant, nonmouse tumors (rat, chicken, man) listed in "Burk's extensive tables" VII and VIII (*7*), many of which were excluded from, or improperly weighted in, the selected and condensed summary prepared by Weinhouse without due regard to the effect of species. This single error in Weinhouse's statistics, by itself, reverses the order of average Q_{O_2} values among his three groups, so that nongrowing > growing > tumor.

The second factor, of equal quantitative importance in tending to widen further the relative difference between normal and tumor tissues, is that in virtually all of the experiments selected by Weinhouse from Burk's tables, simple saline media were employed, instead of sera or similar body fluids that are much more physiological and therefore much more pertinent for the solution of the problem at hand. Extensive modern studies show, even better than earlier studies, that the use of sera instead of saline media increases the average Q_{O_2} values of normal tissues much more than that of tumors—by a relative factor up to 2 and more. This differential response is due partly, though not wholly, to the greater response of normal tissue to respiratory substrates occurring naturally in sera but not added to the early saline media employed in the experiments selected by Weinhouse. This differential response finds equivalent and additional expression in the relatively small succinate oxidative response shown by tumor tissues [impairment type iv; compare Kidd *et al.* (*3*) and Weinhouse (*4*, p. 302)].

It is obvious that in the hands of Weinhouse the statistical approach has led to gross error in final conclusion. This erroneous conclusion has been woven into his papers (*4, 5*) extensively and affects still other conclusions based on it, leading to general confusion not confined to his own papers (*11*).

The error concerning species adjustment that Weinhouse has introduced into his consideration of "Burk's extensive tables" enters with equal force into various of his conclusions concerning his own experimental data (*4, 5*) obtained with isotopically marked substrates, where again results with miscellaneous rat and mouse materials are often mixed indiscriminately; space, however, does not permit tabular detailing of his propagation of errors in this direction. Suffice it to say, his own data reported on Q_{O_2} (sketchy, but republished verbatim many times) show lower average species unadjusted Q_{O_2} values for the tumors (−5.3 for 19 determinations) than for the

normal tissues (−9.5 for 19 determinations) in saline-substrate (nonserum) media. Unfortunately, the mouse data contain only one normal tissue (liver) and several tumor types, whereas the rat data contain only one tumor type (hepatoma) and several normal tissues. If more normal mouse-tissue types and more rat-tumor types had been available for proper species adjustment, the adjusted values (for either species) would have been even wider apart than −5.3 and −9.5, since the Q_{O_2} of hepatoma is relatively high among tumors and the Q_{O_2} of normal liver tissue is relatively low among highly functional normal tissues.

When, in more extensive experimentation, C^{14}-marked substrates were tested (glucose, lactate, acetate, butyrate, octanoate, palmitate, and 2,4-acetoacetate), there was in general a relatively much greater aerobic production of $C^{14}O_2$ by the normal tissue groups than by the tumor groups employed. On an absolute basis, $Q_{C^{14}O_2}$ in the tumors rarely exceeded 2 ("O.C." = 89), and were ordinarily well below 1; but normal tissues ranged up to $Q_{C^{14}O_2} = 4$ and more, notably with lactate, an important constituent of sera. These isotope tracer studies of Weinhouse show that fatty acids and a wide variety of exogenous substrates may be oxidized to carbon dioxide by a miscellany of rat and mouse tumors, but only at quite small initial rates that were on the average lower than the average of initial rates shown by the highly functional normal rat and mouse tissues tested. Such studies largely confirm, albeit with superior quantitative finesse, widely accepted conclusions reached decades ago by investigators who had employed time-honored kinetic, substrate-addition, and respiratory quotient methods.

G. N. Lewis (*12*) has said, "It is a common fault of mankind to refuse to recognize the existence of a phenomenon unless some mechanism has been devised." Much of the general confusion (*11, 13*) evident in the discussion advanced by Weinhouse also derives from his failure to distinguish between various over-all phenomena of respiratory impairment, on the one hand, and detailed mechanisms thereof, on the other. In his own experimental work he has looked for respiratory impairment among details of biochemical respiratory mechanisms, following well-worn channels of possible aberrancy—for example, enzyme content (*14*), citric acid cycle, exogenous substrate oxidation, localized "bottlenecks" in electron transport, pyruvate shunt, hexosemonophosphate shunt, and fluoride and dinitrophenol inhibitions. The results obtained by him, even with isotopic tracers, have in no way contraindicated the over-all phenomena of respiratory impairment, and have indeed provided some valuable supporting evidence. In any event, such conventional and assuredly worthwhile studies are, regardless of outcome, no more essential to experimental recognition of the over-all phenomena of respiratory impairment in living cancer cells than is knowledge of the ultimate physical mechanism of gravitation essential to experimental recognition of the square law of gravitation. In the words of Isaac Newton (*15*), "the main Business of Natural Philosophy is to argue from Phaenomena. . . . we must learn from the Phaenomena of Nature what are the Laws and Properties of the Attraction before we enquire the Cause by which the Attraction is perform'd."

It is a tribute to the genius of Otto Warburg that he discovered the impaired Q_{O_2} of cancers more than 30 years ago with the now obsolete methods and relatively poor (mixed) cancer materials then available, and under the handicap of the statistical approach. It is a further tribute that in recent years Warburg has been the first to appreciate and capitalize on the importance of the use of pure cancer cells (for example, ascites and tissue culture cells) for final decision on the relative status of Q_{O_2} in cancer cells. It should never be forgotten, however, that in the characterization of cancer metabolism, once developed following carcinogenesis, he has always (1924–1956) regarded the invariably high ratio of fermentation to respiration (impairment type i) as of much greater significance than the usually low Q_{O_2} (impairment type ii).

On the basis of impairment type i, and as a confirmatory qualitative demonstration thereof, the following simple manometric test has been devised (*16*) that permits investigators to distinguish cancer cells from virtually all normal body cells, growing or nongrowing. The cells under test are placed in a manometric vessel of any convenient size. The vessel is filled to one-third to one-half of its volume with physiological serum or other equivalent body fluid (5 percent CO_2 in O_2 or air as appropriate, slight alkalinity, adequate glucose and bicarbonate). The volume of cells is of the order of 1/300 the volume of serum. Cancer cells cause the manometer to register a steady and notable increase in pressure with time (minutes to hours), whereas normal (uninjured) body cells cause a negative (or ~ zero) change in pressure with time. The few—if any—exceptions extant are only apparent, or are readily ruled out on other bases; thus, use of nonphysiological media (for example, unfortified saline) may vitiate the test for normal cells, and omission of the carbohydrate glucose certainly will for cancer cells.

This test can be made quantitative, but in the simple form just outlined it possesses the advantage of being qualitative. It offers a distinction between neoplastic and normal cells that is as qualitative as "plus versus minus" or "up versus down," and that is observable in terms of mere pressure change—that is, directional movement of the manometric fluid. The quantitative metabolic basis for the observed qualitative manometry is completely understood. Thus, the sign and magnitude of the pressure change can be expressed as an exact mathematical function of the ratio of the absolute magnitude of aerobic glycolysis to the absolute magnitude of respiration for any given conditions of experimental arrangement (*17*).

It is hoped that this simple test may prove useful or definitive in studies of many tissues or cells of questionable malignancy—for example, in tissue cultures of originally normal cells that are undergoing or have undergone carcinogenesis, as well as numerous *in vivo* instances. In any event, the proposed test is a *post facto* epitomization of three decades of experimental protocols in the literature that are in harmony with the concepts recapitulated in this communication on respiratory impairment in "THE metabolism of THE cancer cell."

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1. O. Warburg, *Biochem. Z.* **142**, 317 (1923); *Metabolism of Tumors*, translated by F. Dickens (Constable, London, 1930); *Science* **123**, 309 (1956); *Science*, this issue.
2. Various words expressing "impaired" respiration have been employed by various writers, all, however, to much the same gross end result, semantics aside: damaged, destroyed, defective, diminished, disturbed, eliminated, harmed, inadequate, inhibited, injured, insufficient, limited, restrained, uncoupled, weakened, *eingeschränkt, entkoppelt, gehemmt, geschädigt, insuffizient, unzureichend, vergiftet, vermindert, zerstört, zugrunde gegangen,* and *zurückgegangen.* In any event, the irreversible respiratory limitation referred to in cancer cells is always partial, never total; otherwise, their life and continued growth would totally cease, so far as is known.
3. J. G. Kidd, R. J. Winzler, D. Burk, *Cancer Research* **4**, 457 (1944).
4. S. Weinhouse, *Advances in Cancer Research* **3**, 269 (1955); *Science*, this issue.
5. ——, *Antimetabolites and Cancer* (AAAS, Washington, D.C., 1955), p. 1; *Cancer Research* **11**, 585, 845 (1951).
6. Weinhouse's frequently reiterated statement that this view held by him has now come to be held *also by Warburg* is categorically incorrect, as simple inspection of the two recent articles by the latter in *Science* (*1*) will suffice to show, in addition to many others that date back to 1924. Questioned directly regarding the accuracy of this footnote, Warburg has provided written, emphatic confirmation (July 1956).
7. D. Burk, *Cold Spring Harbor Symposia on Quant. Biol.* **7**, 437, 441 (1939).
8. H. A. Krebs, *Metabolism and Function* (Elsevier, Amsterdam, 1950), p. 249.
9. E. F. Adolph, *Science* **109**, 579 (1949).
10. It is important to note that the Q_{O_2} values for the mouse tumors of Crabtree and Murphy and Hawkins (1925–29), selected by Weinhouse from Burk's tables and averaging −13.9 for ten types, are, in fact, *exceptionally high* when compared with most values for mouse tumors obtained during the last 25 years by others using improved manometric methods. In the work of Dickens and Simer in 1930–31 (also cited in Burk's tables) the Q_{O_2} values

for the five mouse tumor types reported on averaged only −7.1! Three of these types (sarcoma 37S, tar carcinoma 2146, and spindle-cell tar tumor 173) had an average Q_{O_2} of −5.6, compared with −16.6 for the *same* tumor strains as measured by Crabtree and used by Weinhouse. Thus, even the *unadjusted* average tumor Q_{O_2} value employed by Weinhouse (−11.8) is, as the result of unwarranted bias in selection and incomplete utilization of available data, much too high.

11. Weinhouse's confusion is infectious, although mainly among investigators who do not themselves perform laboratory experiments on cancer metabolism. One may read, for example, "We hear about THE metabolism of THE cancer cell. Unfortunately, no such phenomenon has been established. . . . As Dr. Weinhouse said at the opening of the symposium, the critical difference between metabolism in malignant tissues and in normal tissues does not appear to reside in the major ways in which they handle carbohydrate metabolism." [*Antimetabolites and Cancer* (AAAS, Washington, D.C., 1955, pp. 305, 308)]. Such statements could scarcely be more incorrect or uninformed. They set the clock back and encourage the empirical approach to the problem of cancer by a sheer and vicarious denial of available fundamental information.
12. G. N. Lewis, *The Anatomy of Science* (Yale Univ. Press, New Haven, Conn., 1926), p. 171.
13. In paragraphs 4, 5, and 6 of his note in this issue of *Science*, Weinhouse asks or raises several questions that have been asked, discussed, and answered many times in the literature of cancer.
14. The mechanism of the cancer respiratory impairment may indeed often involve lowered content of a particular respiratory enzyme, but this is not a necessary general requirement, since internal cellular arrangement and chemical or structural restraint of other correlated enzymes are, as in so many living phenomena, often of more decisive importance. Thus, certain ascites cancer cells have been found [B. Chance and L. N. Castor, *Science* 116, 200 (1952)] to have unusually high contents of cytochrome *c*; but even in such ascites cells, the paraphenylenediamine and succinate oxidative responses are characteristically low or zero (*1*, p. 314); this is clearly indicative of respiratory restraint in spite of abnormally high absoute content of cytochrome *c* (compare *4*, pp. 295–6). Oxidation-reduction potential restraints may well be involved here, as well as low contents of cytochrome *b* or DPNH demonstrated.
15. I. Newton, *Opticks* (W. and J. Innys, London, ed. 2, 1718), pp. 344, 351.
16. Presented orally at the 1956 meeting of American Association for Cancer Research. [*Proc.* 2, 98 (Natl. Inst. of Health Information Release, 13 Apr.)].
17. A description of these quantitative potentialities and other qualitative aspects is in preparation.

2 July 1956

On the Biosynthesis of the Porphyrinlike Moiety of Vitamin B_{12}

The investigations performed during the past decade have elucidated many of the intimate biosynthetic steps by which the cell elaborates the porphyrin molecule. It has been found that "active" succinate (*1*) and glycine (*2*) are the sole precursors of the porphyrin compounds in all biological systems studied. The glycine and succinate condense to form α-amino-β-ketoadipic acid. This β-keto acid on decarboxylation yields δ-aminolevulinic acid (*3*). Condensation of 2 mole of the aminoketone results in the formation of the precursor monopyrrole, porphobilinogen (*4*). Four mole of this pyrrole then condenses to form a porphyrin, and modification of the side chains in the β-positions gives rise to a particular porphyrin.

The chemical work of the Merck group (*5*) and of the English workers (*6*) and the x-ray studies of Hodgkin *et al.* (*7*) have culminated recently in the proposal of a very probable structure of vitamin B_{12} which contains a porphyrinlike structure (*6*, *7*). Although this latter component of the vitamin differs somewhat in structure from that of porphyrins (that is, the vitamin molecule contains one pyrrolidine and three pyrroline rings, a methyl group on two of the bridge-carbon atoms, four extra methyl groups in the β-positions of the rings, and an α-methyl group instead of a bridge-carbon atom), there are sufficient similarities to lead to the suspicion that the basic mechanism of synthesis of this part of the vitamin is similar to that known for porphyrins. It would seem possible that the porphyrinlike moiety of the vitamin is synthesized by the mechanism known for pyrrole and porphyrin synthesis and that the modified structure is subsequently methylated in the afore-mentioned positions to form the final product. This conclusion, of methylation subsequent to ring formation from δ-aminolevulinic acid (*6*), is supported by structural considerations. If a methylated derivative of δ-aminolevulinic acid were the precursor, one would expect that the extra methyl groups would be on only those β-positions that bear acetic acid side chains. However, this is the case with only rings A and B; in ring D the methyl group is attached to the carbon atom that bears the propionic acid group.

In order to check this hypothesis, we have carried out a microbiological synthesis of vitamin B_{12} in the presence of 125 mg of δ-aminolevulinic acid-1,4-C^{14} having a molar activity (*1*) of 8.3×10^5 count/min for each active carbon. The culture was agitated in a medium containing the following nutrients, in addition to the δ-aminolevulinic acid: sucrose, 8.75 g; L-glutamic acid, 2.5 g; $(NH_4)_2HPO_4$, 0.5 g; Na_2SO_4, 0.5 g; KCl, 0.2 g; $MgSO_4 \cdot 7H_2O$, 0.125 g; $MnSO_4 \cdot 4H_2O$, 0.05 g; $FeSO_4 \cdot 7H_2O$, 0.005 g; $ZnSO_4 \cdot 7H_2O$, 0.005 g; and $Co(NO_3)_2 \cdot 6H_2O$, 0.01 g. Under these fermentation conditions, the culture produced 0.163 mg of vitamin B_{12}. After the addition of 10.1 mg of nonradioactive B_{12}, 6.294 mg of B_{12} was isolated. The molar activity of the undiluted B_{12} was 30×10^5 count/min. Therefore, in the unlikely possibility that endogenous synthesis of aminoketone be disregarded, at least four carbon atoms of the vitamin must have contained C^{14}.

On the reasonable assumption, based on previous studies on porphyrin formation, that 2 mole of aminoketone is utilized for each ring, one can postulate that 15 labeled carbon atoms (16 minus the carboxyl lost from ring C) of the porphyrinlike structure of the vitamin were derived from our labeled substrate. On this basis the molar activity of each of these 15 carbon atoms would be 2×10^5 count/min. This represents a mere fourfold dilution of the radioactive carbon atoms of the labeled substrate in the course of the synthesis of the vitamin. It may therefore justifiably be concluded that the porphyrinlike structure of vitamin B_{12} is synthesized from δ-aminolevulinic acid, as are the porphyrins, and that the mechanism of synthesis of the ring system in the vitamin is similar to that of the porphyrins.

We are presently engaged in degrading the labeled vitamin in order to isolate those carbon atoms which we predict should contain all the radioactivity.

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28 May 1956

Cell-Wall Mannan-Protein of Baker's Yeast

In isolated cell walls of baker's yeast, Northcote and Horne (*1*) demonstrated the presence of two polysaccharides, an outer glucan envelope and an inner mannan component. Associated with the latter was nitrogenous material. This material was assumed to be protein on the basis of the detection (by chromatography) of amino acids in the products of its partial hydrolysis. The glucan was subsequently shown (*2*) to comprise about 10 percent, and mannan 15 to 17 percent, of the dry weight of baker's yeast. The wall constituents accounted

for approximately 30 percent of the dry weight of the cells.

By mechanical disruption of baker's yeast and its differential centrifugation in media of differing density, preparations of isolated cell walls have been obtained that are entirely free from intact cells and from other particulate cellular matter. From the clean cell-wall fragments, we have isolated a mannan-protein complex (*3*) that appears to be a major structural entity of the cell.

Cells from starch-free pound cakes of baker's yeast (*4*) suspended in water or in a 5 percent (by volume) aqueous solution of thiodiglycol (150 g of yeast, 50 ml of solution) were disrupted in the cold by agitation in a Waring Blendor with glass beads according to the method of Lamanna and Mallette (*5*). More than 90-percent breakage of cells was achieved after 90 minutes of agitation. Cell-wall fragments were isolated by differential centrifugation and repeated washing with distilled water, 8.5-percent sucrose solution, and phosphate buffer (*p*H 7.4, 0.1*M*). Washing with sucrose and with buffer served to eliminate completely the small particles which, in water, sediment along with cell-wall fragments.

After about 50 repetitions of washing and differential centrifugation, a fraction consisting exclusively of cell-wall material was obtained. This was lyophilized. All data are based on material prepared in this manner. By this method of preparation, it is possible to obtain a cell-wall fraction of constant composition. From two different batches of yeast, the nitrogen contents of the cell-wall preparations were 1.28 and 1.24 percent. These values are lower than that (2.1 percent) reported by Northcote and Horne, who stated that their preparation contained no unbroken cells but was contaminated by small particles which were difficult to eliminate.

Table 1. Composition of isolated cell wall of baker's yeast.

Component	Percentage by weight of dry cell wall
Total reducing sugar	84.4
Hexosamine	2.7
Total nitrogen	1.28
Hexosamine N	0.21
Protein N	1.07
Protein N (×6.25)	6.7
Phosphorus	0.34
Sulfur	0.14

The analytic data presented in Table 1 show that the clean cell-wall material contains 6.7 percent protein, 84.4 percent total reducing sugar (anthrone method, *2*), and 3.0 percent chitin (based on the hexosamine content). The high sulfur-to-protein ratio (2.1 percent) indicates that the protein may be of a pseudokeratin type (*6*). By means of paper chromatography of hydrolyzates of cell-wall material, the presence of 15 amino acids and one as yet unidentified substance was demonstrated (Fig. 1).

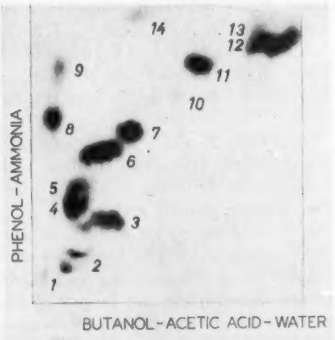

Fig. 1. Amino acids in hydrolyzates (6*N* HCl for 16 hours at 110°C) of isolated cell wall of baker's yeast as demonstrated by two-dimensional paper chromatography (solvents were a solution of butanol, acetic acid, and water and a solution of phenol and ammonia; ninhydrin development; cobalt chloride spray to intensify color and make record permanent): *1*, cysteic acid; *2*, aspartic acid; *3*, glutamic acid; *4*, serine; *5*, glycine; *6*, threonine; *7*, alanine; *8*, lysine; *9*, arginine; *10*, tyrosine; *11*, valine and methionine; *12*, leucine and isoleucine; *13*, phenylalanine; *14*, unidentified. Small amounts of hexosamine present were not detectable after vigorous hydrolysis.

From preparations of clean cell-wall materials a major fraction (approximately 75 percent) was solubilized in 1*N* KOH on slight warming. The solubilized material was dialyzed against running tap water for 24 hours and then lyophilized, yielding a white powder, of which the major part was readily soluble in water. The residue formed a gel that was separated from the solution by centrifugation at 20,000*g*. The nature of this fraction is under study; it appears to be a glucan-protein. (Only glucose is found, in addition to amino acids, after acid hydrolysis). The water-soluble material that had resisted dialysis was found to contain mannan and protein, as shown by analysis for tyrosine (Folin) and polysaccharide (anthrone), ultraviolet absorption at 280 mμ and chromatographic analysis (Only mannose is found, in addition to amino acids, after acid hydrolysis.) Nucleic acid was absent as judged by absorption at 260 mμ. Three different preparations had nitrogen contents close to 1.10 percent (equivalent to 6.8 percent protein).

The mannan and protein appeared to be tightly bound, for the polysaccharide could not be precipitated as the copper complex by treatment with cold Fehling's reagent (*7*). In the ultracentrifuge, the mannan-protein appears to be monodisperse, giving at this stage of purification a sedimentation constant (uncorrected) of $S_{20} = 4.3 \times 10^{-13}$ at several concentrations in water and in buffer (*8*). The mannan-protein complex has been further purified by precipitation from aqueous solution on saturation with ammonium sulfate followed by dialysis and subsequent lyophilization. The amino acid composition of this material is being analyzed quantitatively, and biochemical, immunochemical, and physical studies on the mannan-protein are underway.

From fresh bottom yeast (brewer's yeast) Lindquist (*9*) obtained, by simple agitation of a thick suspension at room temperature, a material which he termed "cebrosan" that has some features in common with the mannan-protein we have isolated. Lindquist reported his purified material contained 1.2 percent nitrogen, but it had the property of a yeast mannan—that is, it was precipitable by Fehling's solution in the cold. The material we have isolated appears to be an almost homogeneous structural entity of the cell wall, consisting of protein and mannan in the ratio (by weight) of 1/12. Evidence has been obtained that this cell-wall protein plays a role in cellular division (*10*).

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Inhibitory Mechanism of Chlortetracycline on D-Amino Acid Oxidase

Yagi *et al.* (*1*) found that *p*-aminosalicylic acid quenched the fluorescence of riboflavin in aqueous solution by the formation of a complex and that the inhibitory action of *p*-aminosalicylic acid on D-amino acid oxidase is partly due to the complex formation between

p-aminosalicylic acid and flavin adenine dinucleotide.

After these results were obtained, many organic substances were examined in our laboratory to determine whether they had a quenching action on flavins. Chlortetracycline was found to be a strong quencher. First the *p*H-fluorescence curve of chlortetracycline was examined. No fluorescence was observed below *p*H 7.0, and the blue fluorescence was strengthened with increasing *p*H values. Therefore in the experiments reported here, the *p*H was fixed at 6.0, a value at which chlortetracycline has no fluorescence but flavins have yellow fluorescence. Chlortetracycline (*2*) and flavin adenine dinucleotide, prepared by the method of Yagi *et al.* (*3*), were dissolved in water and mixed with phosphate buffer. The fluorescence was measured at 20°C, using a fluorometer designed by us (*4*).

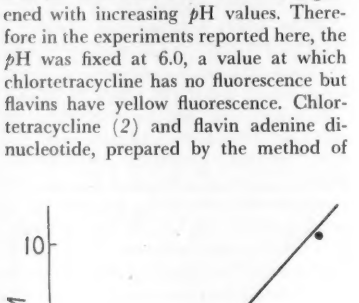

Fig. 1. Quenching of fluorescence of flavin adenine dinucleotide by chlortetracycline. The quantities, f and $(f-x)$, correspond to the intensity of fluorescence of flavin adenine dinucleotide in the absence and presence of chlortetracycline, and x was calculated from these values.

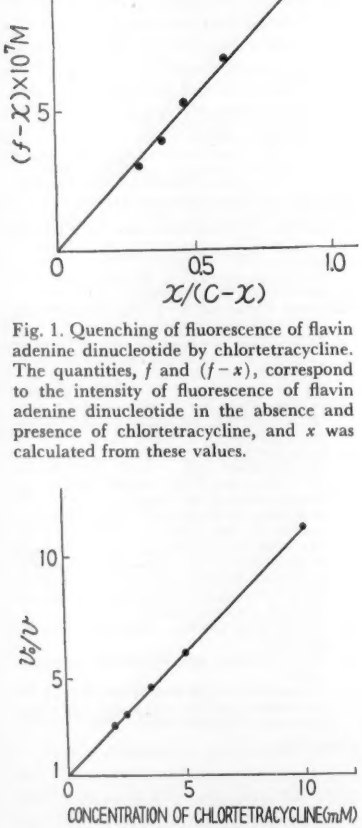

Fig. 2. Inhibition of chlortetracycline on D-amino acid oxidase. Each cup contained 2 mg of oxidase protein and $6.25\times10^{-2}M$ (final concentration) of DL-alanine. After the equilibrium temperature was reached, $1.6\times10^{-7}M$ (final concentration) of flavin adenine dinucleotide and graduated concentrations of from $2\times10^{-8}M$ to $1\times10^{-2}M$ of chlortetracycline were added from the side vessel simultaneously. V was 143 μlit/30 min and v_0 was 87.5 μlit/30 min.

Assuming that the complex is nonfluorescent and that the reaction is bimolecular, the dissociation constant K of the complex will be presented by the following formula.

$$K=\frac{(f-x)\ (c-x)}{x}$$

where f is the molar concentration of flavin adenine dinucleotide, c is that of chlortetracycline, and x is that of the complex in the tested solution. In the measurements, f and $(f-x)$ correspond to the intensity of fluorescence in the absence and presence of chlortetracycline, respectively. Each tested sample contained $1.5\times10^{-6}M$ of flavin adenine dinucleotide and graduated concentrations from $1\times10^{-6}M$ to $5\times10^{-6}M$ of chlortetracycline. When $(f-x)$ was plotted against $x/(c-x)$, a straight line was obtained, as is shown in Fig. 1, and the value of K as calculated from the slope of this line was $1.1\times10^{-6}M$.

The influence of the complex formation by chlortetracycline of a complex with flavin adenine dinucleotide on the activity of D-amino acid oxidase was then analyzed with purified oxidase protein (protein E), which was prepared from hog kidney by the method of Negelein and Brömel (*5*), using a Warburg manometer. The relationship between the activity of D-amino acid oxidase and the flavin adenine dinucleotide concentration is

$$v=\frac{Vf}{K_F+f}$$

where v is the reaction velocity in the presence of a concentration f of flavin adenine dinucleotide, V is the maximum velocity obtained by increasing the concentration of flavin adenine dinucleotide, and K_F is independent of f and v. Using this formula, the dissociation constant of flavin adenine dinucleotide with oxidase protein was calculated as $1.1\times10^{-7}M$.

If chlortetracycline forms a complex with flavin adenine dinucleotide or competes with the latter to combine with oxidase protein and $K\gg K_F$, the activity of the enzyme can be shown as

$$v=\frac{Vf}{K_F\left(1+\frac{i}{K}\right)+f}$$

where i is the concentration of chlortetracycline, K is the constant of its dissociation from a complex with oxidase protein or with flavin adenine dinucleotide. Therefore, K can be evaluated from the following formula as described by Burton (*6*):

$$\frac{v_0}{v}=1+\left\{1-\frac{v_0}{V}\right\}\frac{i}{K}$$

where v_0 and v are the reaction velocity in the absence and presence of chlortetracycline, respectively.

In the experiments, chlortetracycline and flavin adenine dinucleotide were placed in the side vessel of the manometer flask. When, after a temperature equilibrium had been reached, the contents of the side vessel were emptied into the main chamber containing oxidase protein and DL-alanine, the inhibiting effect of chlortetracycline on the reaction velocity was demonstrated. Measured values of v_0/v, plotted against the concentration of chlortetracycline, gave the straight line shown in Fig. 2, which indicated that only one inhibitory factor was present. From the line's slope, K was calculated to be $3.9\times10^{-4}M$. This inhibition may be considered to be due to the formation of a complex by chlortetracycline with flavin adenine dinucleotide.

The difference in the value for K obtained by fluorescence measurement and the value for K obtained by enzymatic research may be attributed to variation in *p*H and temperature. Therefore, $3.9\times10^{-4}M$, the value obtained for K, is considered to be the constant of the dissociation of chlortetracycline from its complex with flavin adenine dinucleotide at *p*H 8.3 and 38°C in the presence of the enzyme. The values obtained for v_0/v when, after incubation of oxidase protein, DL-alanine, and chlortetracycline in the main chamber for 10 minutes, flavin adenine dinucleotide was added from the side vessel nearly agreed with those shown in Fig. 2. However, each value obtained closely approached 1 when, after oxidase protein, DL-alanine, and flavin adenine dinucleotide had been incubated in the main chamber for 10 minutes, chlortetracycline was added from the side vessel.

From these results, it may be supposed that chlortetracycline can combine with flavin adenine dinucleotide when it is free from oxidase protein and cannot react with flavin dinucleotide when it is combined with protein. The formation of a complex by chlortetracycline with flavin adenine dinucleotide may be one of the factors in the etiology of the ariboflavinosis that is caused by this antibiotic.

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7 May 1956

Chondroitin Sulfate and Hyaluronic Acid in Syphilomas of Cortisone-Treated Rabbits

In a recent publication (*1*) Turner and Hollander cited certain of my conclusions regarding the identity and relative concentration of chondroitin sulfate and hyaluronic acid in rabbit syphilomas. I want to report here the experimental evidence on which these conclusions were based (*2*).

The sulfated and nonsulfated polysaccharides were extracted from the syphilomas (*3*) of cortisone-treated and untreated animals and separated by a modification of the method of Pearce and Watson (*4*). The properties of the polysaccharides were then compared with those of the corresponding polysaccharides from normal skin.

The syphilomas were excised from the back of the rabbit (*1*), freed from hair and apparently normal skin, ground with sand in a mortar, and extracted with 10 ml of 2.5*N* sodium hydroxide for 24 hours at 35°C. After centrifugation the supernatant fluid was filtered through a 1-cm layer of Celite on a fritted glass funnel. The insoluble portion was reextracted four times with 10-ml quantities of distilled water and separated by filtration through Celite on a fritted glass funnel. The combined alkali and aqueous extracts were neutralized with glacial acetic acid (*p*H 7), treated with Lloyds reagent, filtered, and treated with an amyl alcohol-chloroform mixture to remove protein (*5*), and the polysaccharides were precipitated from the aqueous phase by the addition of 20 vol of ethanol. The precipitate was washed with ethanol and with ether, dried under a high vacuum at room temperature, and then redissolved in distilled water containing excess barium acetate. The solution was filtered and fractionated into sulfated and nonsulfated polysaccharides by the addition of ethanol to a concentration of 20 and 80 percent (*4*), respectively. The precipitate was collected by centrifugation, washed with ethanol and with ether, and dried under a high vacuum over phosphorus pentoxide.

Table 1 shows that, analytically, the sulfated polysaccharide of rabbit syphilomas is indistinguishable from chondroitin sulfate. The optical rotation indicates that it is the chondroitin sulfate C of Meyer and Rapport (*6*). The nonsulfated fraction is analytically the same as hyaluronic acid.

If we consider the quantities of chondroitin sulfate and hyaluronic acid isolated (Table 2), it is apparent that, although there is no marked difference in the relative concentrations in the syphiloma compared with normal skin, there is a threefold decrease in the chondroitin sulfate as compared with the hyaluronic acid after cortisone treatment. Although it is unlikely that the polysaccharides were quantitatively isolated, the relative amounts found should directly reflect the relative concentrations of the polysaccharides in the tissues.

Hyaluronic acid is frequently found in greatly hydrated gels and is apparently involved in water binding (*7*); hence, it is not too surprising to find an increase in the hyaluronic acid content of the soft hydrated syphilomas that are produced in the cortisone-treated animal as contrasted with the relatively water-free lesions of the untreated animal.

Various diseases and experimental conditions give rise to an increase in the concentration of mucopolysaccharide material. Such an increase is found in rheumatoid arthritis (*8*), in the Aschoff bodies of rheumatic fever, in myocarditis, in acute rheumatic carditis (*9*), and in the skin or coxcomb of experimental animals after the application of sex (*10*) or pituitary (*11*) hormones. The formation of dense collagen fibers, as shown by investigations on human skin (*12*), is accompanied by a relative drop in the ratio of hyaluronic acid to chondroitin sulfate. Layton has demonstrated (*13*) that cortisone inhibits sulfated-polysaccharide synthesis.

Table 1. Identity of the polysaccharide fractions that were isolated from the syphilomas of cortisone-treated and nontreated animals with chondroitin sulfate and hyaluronic acid.

Item	Chondroitin sulfate*				Hyaluronic acid			
	Hexosamine (*14*)	Nitrogen	Sulfur	$[\alpha]^{20}_D$	Hexosamine (*4*)	Nitrogen	Sulfur	$[\alpha]^{20}_D$
Cortisone-treated	25.4	3.96	3.4	−18°	28.1	3.3	0.0	−65°
Untreated	25.6	3.94	3.1	−18°	28.5	3.4	0.0	−65°
Normal skin	25.7	3.9	3.1	−18°	28.5	3.3	0.0	−64°
	29(*15*)	3(*15*)		−19°(*16*)				
Reported	31(*17*)	5(*16*)	2–4(*16*)	−20°(*5*)	30–40(*18*)	3–3.5(*19*)	0.0	−70°(*5*)

* Analyses obtained on the barium salt were recalculated for the potassium salt.

Table 2. Weight of chondroitin sulfate and hyaluronic acid isolated.

Source	Weight of tissue (g)	Chondroitin sulfate (mg)	Hyaluronic acid (mg)	Chondroitin sulfate/hyaluronic acid
Cortisone-treated*	20.1	205	532	0.4
	10.7	111	218	0.5
Untreated	4.5	100	79	1.3
	2.1	50	41	1.2
Normal skin	8.1	14.4	10	1.4
	10.0	16.4	10	1.6

* Six syphilomas excised from the back of one rabbit (*1*).

I suggest that the action of cortisone on the developing syphiloma is to inhibit the incorporation of sulfate into certain hyaluronic acid or hyaluronic acidlike polysaccharides produced by the animal tissue in response to the mechanical or biochemical stimuli of the treponeme. As a consequence, the relative concentration of nonsulfated polysaccharides or hyaluronic acid is increased; this, in turn, leads to a retention of water in the syphiloma.

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5 June 1956

Letters

Batteries in England

I was interested in the editorial comments [*Science* **123**, 1059 (15 June 1956); 1099 (22 June 1956)] to the effect that the "customer's" appraisal of a product can be very different from the scientific evaluation, and that the difference may persist even when the result of the scientific evaluation is known.

You may be interested in a small controversy over batteries that occurred in England in the early 1930's. A columnist in a radio magazine expressed the opinion that some 120-volt dry batteries, then on the market at 5 shillings (when the cost of a similar battery from a reputable manufacturer would have been about 12 shillings), could not be very good. By a simple piece of arithmetic he proved that it could not possibly be economic to market a carefully made battery at less than a penny per cell. In response, he got several letters from people who said that they were using such batteries in their radios with "excellent results" and suggested that "he must be in league with the manufacturers" of the more expensive batteries. He then tested the cheap battery by a series of intermittent discharges through a resistance, designed to represent the effect of ordinary use in a radio set, and compared its performance with that of a more expensive battery. For some weeks he gave in his column a blow-by-blow account of the test and clearly demonstrated that, although the cheap battery worked well at the beginning of each discharge period, its performance fell off rapidly toward the end, compared with the more expensive one, which was just what might have been expected.

The response to this was a crop of letters to the editor, claiming that the writers "had performed similar tests with much better results," etcetera, etcetera. One of them ended: "I think 'Thermion' must have chosen a dud." ("Thermion" was the pen-name of the columnist.) At this "Thermion" gave up the argument in despair, concluding that the intense desire of people to justify themselves (and to "prove" that the reputable manufacturers were making an excessive profit on their batteries) had clouded their judgment, both of the performance they were getting from their radios and of the results they claimed to have been getting on the test-bench.

H. N. V. Temperley
Riversdale, Grantchester, Cambridge, England

What Is Behavioral Science?

The expression *behavioral science* has come into use in recent years. This designation appears to be an outgrowth of the interest of the Ford Foundation in Program V, "scientific activities designed to increase knowledge of factors which influence or determine human conduct, and to extend such knowledge for the maximum benefit of individuals and of society." This area has been repeatedly referred to as "behavioral science" in more recent writings, and recently a journal with this name was founded.

Behavioral science would be equated by some to psychology. Besides limiting behavioral science unduly, this would not suit some psychologists, inasmuch as it would appear to overemphasize the behavioristic approach. The recently instituted journal is an interdisciplinary effort, for the editorial staff includes not only psychologists and psychiatrists but also a political scientist, a neurophysiologist, an economist, a mathematician, and an educationist. The interdisciplinary aspect of this venture seems clearly desirable.

The question that I wish to raise before the term *behavioral science* takes on an unfortunate restricted meaning is that of the status of genetics, biochemistry, and biophysics. My concern is not prompted by a desire to emphasize a mechanistic approach to the subject, but I have real misgivings about attempting to build a superstructure without any concern for the foundation.

It is no secret that the trend in the social sciences is environmentalistic. When it comes to an interdisciplinary study as broad as behavioral science, however, geneticists need to be called into action because no one can question but that there is an interplay between genetic and environmental influences, and that in order to understand either, one must understand both.

Behavioral science certainly has its roots in biology, and the foremost frontiers of biology lie in biochemistry and biophysics. To leave biochemistry and biophysics out of behavioral science is to be superficial and hedge it about on the basis of a priori assumptions which are quite unwarranted. It is preposterous in view of all we know to exclude nutrition and endocrine balances from the "factors which influence or determine human conduct." It would seem very unfortunate just when genetics is beginning to throw light on these subjects to invite it to stay out.

One of my own interests in this field is related not to the uniformity of human behavior but to the nonuniformities. It is interesting to know as much as we can about why people act alike, but it is also worth while (and crucial in my opinion) to know why people *do not behave alike.* Biochemistry has much to offer in the way of insight into this problem, as is brought out in a forthcoming book on *Biochemical Individuality.*

If biochemistry and genetics were minor disciplines and could contribute only in a trifling way to behavioral science, their exclusion would not be so serious. Very recently, in a principal address at the Chicago meeting of the American Psychiatric Association, Percival Bailey, a neurosurgeon, neurologist, and psychiatrist, indicated that future progress in dealing with mental disease is largely in the hands of biochemists. This bears out the crucial need for interdisciplinary study of behavioral science in which biochemistry is an important part. In line with this need, we have recently instituted, with the support of the Welch Foundation of Houston, a cooperative study at the University of Texas and the Austin State Hospital (for mentally ill) in an attempt to discover the biochemical roots of mental disease.

Roger J. Williams
Department of Chemistry and *Biochemical Institute, University of Texas, Austin*

I agree with the point made by Roger J. Williams. The term as it applies to the Center for Advanced Study in the Behavioral Sciences covers all scientific efforts directed toward an understanding of human behavior. Last year, the fellows of the center included three biologists. Among the current seminars is one on the biological bases of human behavior. One of the biologists who will be a fellow next year is a geneticist. Many scientists studying human behavior recognize the interdependence of biochemical, biophysical, and social factors. More

This department will appear occasionally. For suggestions concerning acceptable items, see the editorial in this issue.

studies in these areas are needed and should be encouraged.

Among the difficulties of unraveling these important interrelated factors are those of developing productive interdisciplinary efforts. Biochemistry and biophysics have developed after many years of unrelated work done by biologists, chemists, and physicists. Psychologists, anthropologists, and sociologists have increasing intellectual contact among themselves but carry on little intensive work with biochemists and biophysicists. I hope that the kind of cooperative study mentioned by Williams will be one of many which will pave the way for fruitful interdisciplinary work involving scientists from both biological and social fields.

RALPH W. TYLER
Center for Advanced Study in the Behavioral Sciences, Stanford, California

Postnatal Determination of Sex

It is a pity that John R. Baker could not have seen the 30 Mar. issue of *Science* before writing his excellent article on "English style in scientific papers," [*Science* **123**, 713 (27 Apr. 1956)]. I refer, of course, to the article on the detection of sex of fetuses [*Science* **123**, 542 (30 Mar. 1956)], specifically the sentence on page 543: "The sex of the newborn infant has been established on the basis of external physical examination." Out here, we use the colorimetric method: pink bootees = boy; blue = girl.

JAMES J. DOHENY
Chicago Section, American Chemical Society

To forestall other letters on this subject, the editors ask readers to note that the custom of using pink for boys and blue for girls is apparently not standardized: in some places, it is reversed.

Michurin, Vavilov, and Lysenko

As a supplement to G. L. Stebbins' recent report on the "New look in Soviet genetics" [*Science*, **123**, 721 (27 Apr. 1956)], I would like to draw attention to another article in *Botanicheskii Zhurnal* the Soviet Russian journal which also contained the material cited and discussed by Stebbins. This article [**40**, 752 (Sept.–Oct. 1955)] is written by P. A. Baranov and D. V. Lebedev on the occasion of the 100th anniversary of the birthday of Michurin and bears the title "Forgotten pages from the biography of I. V. Michurin: I. V. Michurin and N. I. Vavilov."

It is generally known to those who have followed the development of the "Soviet genetics" that Lysenko and his followers have claimed Michurin as their spiritual forerunner and have insisted that Michurin's work was not appreciated and was even suppressed by the "professional" geneticists. According to their story, it took the personal interest and intervention of Lenin to provide Michurin with adequate support for his work, and it later took the genius of Lysenko himself to recognize fully the significance of this work.

Baranov and Lebedev, however, show in their article that Michurin's breeding work not only had attracted the attention of "professional" botanists as early as the time of Czarist Russia, but that it was none other than N. I. Vavilov who initiated the support Michurin received in the last 12 or 15 years of his life. The two men first met in 1920, and Vavilov was sufficiently impressed with Michurin's achievements in fruit breeding to request a report and induce the government—quite likely Lenin personally, who at that time indeed took great interest in the improvement of plant breeding in Russia—to provide Michurin with an experiment station of his own and with adequate funds. The two men remained in contact for the rest of Michurin's life. Shortly before the latter's death, Vavilov sponsored his election to honorary membership in the Soviet Academy of Science.

Baranov and Lebedev emphasize that Vavilov did not agree with all of Michurin's ideas. There can indeed be little doubt that he had no use for the Lamarckian concepts in Michurin's theoretical work or for such notions as the "mentor theory," according to which compatibility of species, and so on, can be modified by graft union. But he was attracted by two features in Michurin's breeding work in which Michurin was without question ahead of most plant breeders of that time, namely, the use of species hybrids and the utilization of the world's resources of cultivated plants. The latter, of course, was one of Vavilov's own main interests, and Vavilov was ready from the first to recognize Michurin's practical accomplishments, such as the breeding of fruit varieties that could be grown in regions that nobody had ever considered for raising fruit.

On the other hand, Baranov and Lebedev cite passages from the writings of Michurin which show that Michurin was far from considering his theoretical contributions as something incontrovertible and final. On the contrary, he stated specifically, and on more than one occasion, that he did not claim to have refuted the laws of Mendel or the results of other geneticists, and that he might have made mistakes in interpreting these results. Somewhat naively, he added that he did not consider this very serious, since such mistakes would be corrected by future investigators.

Michurin died in 1935. In that year, Lysenko, although in the ascendancy, was still a long way from his peak of power. There is no evidence that he has rendered Michurin any actual service, direct or indirect. The only "service" he did render him was to elevate his theoretical notions—proposed in all sincerity, but not supported by any conclusive evidence—to the rank of Soviet biological gospel, thus making Michurin one of the bogus theoreticians of the Soviet system. For the support that Michurin, the successful plant breeder, received in the later part of his life, he was indebted to Vavilov, the man for whose death Lysenko bears the ultimate responsibility. The fact that Vavilov's part in Michurin's career can again be reported in a Soviet Russian journal is another proof of the "new look" in Soviet genetics.

ANTON LANG
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Role of Teachers in Scholarship Programs

On behalf of the Chicago Section of the American Chemical Society, I should like to comment on the letter from H. J. Bennett *et al.* on the "Role of teachers in scholarship programs" [*Science* **123**, 942 (25 May 1956)].

The Chicago Section has for the past 2 years sponsored a scholarship program in which high-school chemistry teachers, at least, far from being "completely overlooked," are recognized along with their students. The program consists of an annual competitive examination in chemistry for high-school students. Not only do the first five winners receive sums ranging from $100 to $700 that are applicable to college tuition and fees, but the teacher of each prize winner receives a cash award of $100. The funds for the awards are obtained through solicitation from industry by the section's Endowment Committee, and the examination itself is administered by the section's Education Committee.

No complicated entry forms or screening tests are involved. The teacher merely sends the names of not more than two of his students to the Chicago Section. About 200 students, representing about 150 teachers, have taken the examination each time.

We hope that the number of entrants and the size of the awards can be increased in the near future.

H. S. CONWAY
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Book Reviews

Technical Education. Its aims, organisation and future development. P. F. R. Venables. Bell, London; Essential Books, Fairlawn, N.J., 1955. 645 pp. 42s.

The present problem of an adequate supply of technical and scientific manpower is of a world-wide nature. This book is primarily concerned with the question of technical education in Great Britain. There the field of technical education is regarded as consisting not only of engineering and the physical sciences, but also pharmacy, botany, zoology, building, textiles, plastics, pottery, art, commerce and so forth. Although much of the detailed discussion with respect to the facilities and enrollments of the principal technical institutions, out of the approximately 400 listed, is of minor interest to American technologists, a great deal of educational theory and experience is of mutual interest. Charles Morris has said, "The trouble is that a study of physics and chemistry does not encourage boys to go into industry. It tends to make them hang around laboratories all their lives. The need is to fire the imagination of boys at school with the exciting possibilities of work in the technological field." Such colorful quotations will be received with smiles by many industrial recruiters in this country, because the pressure during the last decade in the United States has been to emphasize greatly the desirability of more physics and chemistry as being the very things that do fire the imagination of the top-level minds.

The book discusses in much detail the course content of British education in engineering, building trades, art, and commerce, as well as the sciences. It will be surprising to American readers to note how very small a fraction of the total enrollment in British technical schools is in the full-time day-student category. A far larger percentage of part-time and night-school students are handled there than in this country.

Some of the early chapters of the book deal extensively with the theory of cooperative courses (called sandwich courses in England), and fairly evaluate the pros and cons of this form of training. Contrary to U.S. belief, the theory of part-time work, part-time study, was originally initiated at the Royal Technical College, Glasgow, about 1880, and the University of Cincinnati was the first in this country, around 1905, to establish co-op. Venables has visited many of the technical schools in this country, including many of our co-op institutions, and he points out the pitfalls as well as advantages for certain classes of students for combined industry-college training as against the more common straight 4-year course of education.

Some of the concluding chapters deal with academic freedom, institutional administration, finance, and student problems. The book will serve as a valuable reference book for technical educators in this country, even though it is doubted that many will feel justified in spending time in reading it completely.

A similar evaluation of American technical education by an equally competent author (or authors) would be very valuable at the present time, and for the near future, during which time there will certainly be an increasing pressure on the part of American industry for a more basically trained man than has been the average engineering product in the past. The present book will serve as an excellent guide for anyone with the energy to do an equivalent job of authorship.

DONALD H. LOUGHRIDGE
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Biochemical Mechanisms in Inflammation. Valy Menkin. Thomas, Springfield, Ill., ed. 2, 1956. 437 pp. Illus. $9.50.

This is the second edition of a monograph published in 1950 under the title, *Newer Concepts of Inflammation*. The first edition consisted of the text of four lectures presented before the Midwest Seminar of Dental Medicine in 1948 to which had been added a series of long and complicated footnotes. The present edition contains three times as many pages as the first. The title has been changed, and most of the footnotes of the first edition have been inserted into the text proper, many of them verbatim. Valy Menkin has added descriptions of more of his own experiments, some old and previously unpublished, others carried out since the appearance of the first edition. The detailed descriptions of Menkin's own experimental studies are irregularly interspersed with sketchy, incomplete, and somewhat superficial reviews of recent work of others in this and closely related fields.

If this book was intended to present another extensive review of Menkin's own investigations, to emphasize his methods and approach in studying inflammation (including fractionation of the exudate and chemical characterization to its components), to plead for general use of the terms he has coined through the years, to catalog the confirmations of his findings and terminology by others, to preserve his claims of priority in suggesting concepts and hypotheses, and to offer a stout, often bitter, defense of his interpretations and evaluations of his own experiments and his ideas of their significance against any and all who have criticized or disagreed with them, its purposes have been accomplished. Furthermore, the book can be recommended without reservation to those whose interests in this field are such as to coincide with Menkin's.

However, for those who purchase the book with the thought that they will obtain a more or less objective and balanced summary of recent investigations of the inflammatory process and its accompanying phenomena, it will be a disappointment. Menkin has omitted or mentioned only briefly several significant studies by others. The text is continually interrupted by violent polemics in which Menkin accuses his critics of having disregarded some one or another of his numerous publications, of having drawn erroneous conclusions from inadequate data, of having failed to support some statement by factual experimental evidence, of misquoting him, of making unwarranted inferences, and especially, of expressing opinions that conflict with his own without having first attempted to duplicate his results using his exact techniques in the same animal species under the same experimental conditions. I found these defenses repetitious, discursive, distractive, and occasionally in poor taste.

Although Menkin frankly states in several places that he has not reviewed or attempted to review all of the recent work in this field, this admission in and of itself cannot be said to enhance the book's value. Furthermore, I in no way deny Menkin's right to publish a defense of his ideas and concepts at any length he may choose. Nor, to be sure, would Menkin deny my right to the opinion that his second edition is not worth its price to those who would purchase the book in the hope that it summarizes in

a useful fashion the present status of experimental studies of capillary permeability, fixation at the inflammatory site, metabolic alterations in inflammatory states, leukopenia, leukocytosis, phagocytosis, fever, mechanisms of tissue injury, hypersensitivity, repair and regeneration, or anti-inflammatory agents. Nor does the monograph fulfill the need for a reliable guide in planning further investigations in any of these fields.

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Rockets and Guided Missiles. John Humphries. Macmillan, New York, 1956. 229 pp. Illus. $6.

John Humphries, one of the outstanding rocket experts in Great Britain, has written a book that is certain to attract wide attention. It is accurate, comprehensive, and easily understandable. Mathematics is used very sparingly and is not essential to the understanding of the major portion of the text. The approach is mainly descriptive.

The author takes up the properties of solid propellant rockets and liquid propellant rockets and discusses specific designs; German, English and American rockets are mentioned. Then there follow sections on missiles in which he considers tracking methods, step-rockets, and the applications of missiles. Here a number of specific guided missiles are discussed in detail, for example, the German V-2. Manned rocket planes are also described, both the research planes used in the U.S. and the antipodal bomber proposed in Germany during the war.

The last section of the book is given up to other rocket applications with only a few pages devoted to space flight. However, applications of rockets are mentioned: torpedoes, rocket-propelled sleds, and so forth. There are more than 120 detailed figures in the book, some very excellent photographs, and a very useful bibliography.

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Solid State Physics. Advances in research and applications. Frederick Seitz and David Turnbull. Academic Press, New York, 1955. xii + 469 pp. Illus. $10.

For the reader who wants to learn all about recent experiments on the homogeneous properties of germanium and silicon, here is an article by H. Y. Fan. Those who were still a little puzzled by the Bohm-Pines theory of electron-electron interactions and plasma oscillations are now given another chance in an article by Pines. Wigner and Seitz collaborate again to give us the latest word on cohesive energies of all the metals.

There are three other articles. F. S. Ham gives a labored account of a relatively new method for finding the logarithmic derivative of the radial wave function outside an ion core in terms of the spectra of the free atom. Is it really necessary to prove that a solution of the radial wave equation satisfying one-point boundary conditions is an integral function of E? The theorem is proved by Ince for a regular end point, and Bôcher (1900) has given a far nicer proof with fewer assumptions than Ham for the singular case. On the other hand, an apparently recent theorem on the normalization of a wave function is only quoted as due to Silverman (1952). (The method appears to be due to Rayleigh, see section 164 and section 203 of his *Sound.*)

J. R. Reitz gives an account of all the methods for finding one-electron wave functions in a periodic potential. The first part of the article is devoted to the classical work on the subject that is readily available in the standard books. And where these standard books so frequently fail, namely in the proof of Bloch's theorem, Reitz also has an incomplete proof; he has neglected the boundary conditions. This article gives me the impression of being a cut-down version of a book on the subject, and I would have much preferred to read the book. I wonder, for example, whether the uninitiated will really appreciate Reitz's comments on Kubic harmonics. Surely, after so much space had been devoted to easily available things, more might have been given to Von der Lage and Bethe. T. Muto and Y. Takagi review experiments on the effects of ordering in alloys on the electric, magnetic, and mechanical properties. In addition, and with little connection, they give the usual treatments of the order-disorder transition from Bragg and Williams to Onsager.

The editors comment that there has been an enormous expansion in solid-state physics since 1940 and that as a result ". . . physicists are finding that, in order to make significant contributions, it is necessary to concentrate . . . in narrower fields than formerly." They believe that this new series will provide "a mechanism whereby investigators and students can readily obtain a balanced view of the whole field." I cannot help but believe that the editors are slightly confused on this point. Surely the student's outlook will not be broadened by reading "compact and authoritative reviews" on small aspects of a subject. On the contrary, the way to obtain a balanced view of all the aspects of a subject is to read a book by one author (or a few authors in close collaboration) which presents a balanced view of the subject.

An obvious example is Wilson's book on transport phenomena. It is with horror, then, that I read of the cavalier dismissal of such books by the editors in their introduction: "Although excellent short texts have recently appeared, many scientists have come to recognize the need for an up-to-date treatise on solid state science that reviews comprehensively all of the important facets of the subject." They go on to say that this is to be the purpose of their new series. It is to be hoped that authors, who could bring a wealth of experience to their writing, will not be content in the future merely to contribute an article to *Solid State Physics,* but will still give us the pleasure of seeing a much divided subject as a whole.

No doubt there will be some facets of solid-state physics that are sufficiently isolated and small that we may expect one good article on them, and I am eagerly looking forward to these. For the rest, I believe that the editors, if they are not going to produce just another review series (and a very expensive one at that), will need to put much more effort into their production. Articles should not appear just by the whim of their authors, but interrelated subjects should appear together, and the authors of these contributions should have had the benefits of consultation with their collaborators. Otherwise, I fear that these volumes will be neither a good review series nor a good *Handbuch,* which is not to say that they will not be much sought after.

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Linear Feedback Analysis. J. G. Thomason. McGraw-Hill, New York; Pergamon, London, 1955. x + 355 pp. $8.50.

Feedback has become an indispensable tool in electronics, communication, servomechanisms, and automatic controls, and this book provides a rather full introduction to it. Intended for the science graduate working in one of these fields, it concentrates mostly on theory. However, a number of design problems are worked out in detail—often accompanied by the kind of practical observations one expects from someone who has had to hunt the "bugs" in a circuit after designing and constructing it.

The first three chapters discuss mesh and nodal network equations, introduce the Laplace transform technique for

solving circuit problems, and apply it to simple examples. The next two give an introductory survey of feedback circuits and a short discussion of amplifier stage design. The next three, on stability of feedback systems, gain-phase analysis, and stabilization techniques, develop the general theory in detail; this is applied in the last three chapters to illustrative feedback amplifiers, feedback integrators and differentiators, and stabilized power supplies. These six chapters, about two-thirds of the book, although they are not as comprehensive in the treatment of theory as the book by Bode or some more recent books, do go far enough to permit the student to design his own circuits on the basis of the principles laid down. The applications are sufficiently varied and numerous to develop a feeling for when feedback techniques can be used advantageously. The clarity of the presentation makes me wish that more applications had been discussed.

American readers may occasionally be bothered by the use, without explanation, of British technical jargon not in common use here. One sometimes wonders at the choice of what is assumed as known to the reader and what is developed in detail—for example, complex variable is developed *ab initio* for the discussion of the Nyquist stability criterion after being assumed in the earlier discussion of Laplace transforms, transfer functions, and so forth. A more extensive bibliography, particularly of applications, would enhance the usefulness of this useful book still further. It is attractively printed and illustrated. Only one nontrivial misprint was noted, namely "cosh ωt" where "cos ωt" should be (entry 14, table of Laplace transforms, page 345.

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Principles and Practice of Field Experimentation. Technical communication 18. John Wishart and H. G. Sanders. Commonwealth Bureau of Plant Breeding and Genetics, Cambridge, England, ed. 2, 1955. 133 pp. 21s.

This small and concise clothbound book will continue to be of considerable value to experimenters even as the first edition was. The material in part II is especially interesting and should be reread periodically by all experimenters who conduct field trials. Consulting statisticians will also find part II enlightening and worth-while reading. The authors state in the preface that "Part I has been almost entirely rewritten in order to make the book suitable for an introductory lecture course on the application of statistical methods to field experimentation, and the material has been expanded to include reference to the more elaborate designs suitable for factorial trials and for use with large numbers of varieties. Part II has been revised and added to."

It is true that part I has been rewritten, but it is unfortunate that the authors did not make use of some of the new developments in statistics by J. W. Tukey, D. B. Duncan, and M. Keuls on comparisons among means. Also, the relationship of error rate basis in experiments, type I error, type II error, and sample size are not considered. In order to be up to date, a book on statistics must consider these topics. The least significant difference (lsd) procedure is used throughout the book and the implication is that the error rate per experiment is 5 percent. This is not so; the error rate per comparison is 5 percent when all comparisons between two means are considered. Using an lsd procedure, the experimenter will find that the error rate per experiment may be larger than desired.

It is felt that the authors could have been more precise in their suggestions for using statistical procedures. Statistics as a science is objective, but the application of statistics becomes somewhat subjective; statisticians should strive to make the application of statistics as objective as possible. The book could be improved in this respect.

The following additional references should have been included: Smith, *J. Agri. Sci.* **28**, 1; Yates and Cochran, *J. Agri. Sci.* **28**, 556; Yates and Zacopanay, *J. Agri. Sci.* **25**, 545; Yates and Hale, *J. Roy. Stat. Soc. B*, **6**, 67; Eisenhart, *Biometrics* **3**, 1; Cochran, *Biometrics* **3**, 22; Bartlett, *Biometrics* **3**, 39; Yates, *Imp. Bur. Soil Sci., Tech. Comm.* 35. Also, a number of the comments by Yates and Zacopanay on techniques of sampling and by Yates (*Imp. Bur. Soil Sci. Tech. Comm.* 35) and Snedecor (*Statistical Methods*) on number of significant figures, rounding errors, and so forth, should have been included in the present version of the book. The inclusion of the aforementioned items would have more than compensated for the additional pages required.

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New Books

Resistance Welding. Theory and use. Prepared by Resistance Welding Committee, American Welding Society. Reinhold, New York; Chapman & Hall, London, 1956. 163 pp. $4.50.

A Follow-Up Study of War Neuroses. Norman Q. Brill and Gilbert W. Beebe. Supt. of Documents, GPO, Washington 25, 1956. 393 pp.

Infinite Sequences and Series. Konrad Knopp. Translated by Frederick Bagemihl. Dover, New York, 1956. 186 pp. Paper, $1.75.

Advances in Chemical Engineering. Thomas B. Drew and John W. Hoopes, Jr. Academic Press, New York, 1956. 448 pp. $10.

CIBA Foundation Symposium on Extrasensory Perception. G. E. W. Wolstenholme and Elaine C. P. Millar. Little, Brown, Boston, 1956. 240 pp. $6.

Taboo. Franz Steiner. Philosophical Library, New York, 1956.

Essentials in Problem Solving. Zuce Kogan. Arco, New York, N.Y., 1956. 119 pp. $3.

Earth Satellites as Research Vehicles. Proceedings of the symposium held 18 Apr. 1956 at the Franklin Institute in Philadelphia. Monograph No. 2. Journal of the Franklin Institute, Philadelphia, Pa., 1956. 115 pp. $2.50.

Report of the Special Committee on the Federal Loyalty-Security Program of the Association of the Bar of the City of New York. Dodd, Mead, New York, 1956. 301 pp. $5.

Science and Civilisation in China. vol. 2. *History of Scientific Thought.* Joseph Needham. Wang Ling, research assistant. Cambridge University Press, New York 22, 1956. 696 pp. $14.50.

Geology and Ourselves. F. H. Edmunds. Philosophical Library, New York, 1956. 256 pp. $10.

Chemistry and Uses of Pesticides. E. R. de Ong. Reinhold, New York; Ch pman & Hall, London, ed. 2, 1956. 334 pp. $8.75.

Miscellaneous Publications

(Inquiries concerning these publications should be addressed, not to Science, *but to the publisher or agency sponsoring the publication.)*

The Hazards to Man of Nuclear and Allied Radiations. Presented by the Lord President of the Council to Parliament by Command of Her Majesty June 1956. Medical Research Council. Her Majesty's Stationery Office, London, 1956. 128 pp. 5s. 6d.

Psychiatry, the Press and the Public. Problems in communication. American Psychiatric Association, Washington, D.C., 1956. 66 pp.

Manpower and Education. Educational Policies Commission. National Education Association, 1201 16 St., NW, Washington 6, D.C. 128 pp. $1.25.

Current Issues in Higher Education, 1945, Resources for Higher Education. Proceedings of the 11th annual National Conference on Higher Education. Chicago, Ill., 5–7 Mar. 1956. G. Kerry Smith, Ed. Association for Higher Education, 1201 16 St., NW, Washington 6, D.C. 363 pp. $4.

Fédération Internationale des Traducteurs F.I.T, Premier Congrès Mondial de la Traduction. Rome, 29 Feb.–1 Mar. 1956. Associazione Italiana Traduttori, Via Firenze, 15, Rome, 1956. 44 pp.

Carver Foundation, Tuskegee Institute, Alabama, Annual Report 1954–55, Ten Years of Research. Carver Foundation, Tuskegee Institute, Ala., 1956. 18 pp.

Meetings and Societies

Marine Biology

Under the auspices of the International Union of Biological Sciences and sponsored by the University of California, Scripps Institution of Oceanography, and the Office of Naval Research, there was held 23 Mar.–2 Apr., at La Jolla, Calif., a symposium on "Perspectives in marine biology," with 47 participants, about 72 observers, plus Scripps personnel. Adriano Buzzati-Traverso organized the program, took the brunt of intricate diplomatic problems, and directed the large staff in managing a complex function.

The main strength and the main weakness of the conference may be said to have derived from the large number of people and the great diversity of disciplines represented. A high percentage of the members were not marine biologists. Many fields, but especially ecology, physiology, genetics, and evolution were represented. The advantages of this feature were felt by the members of these disciplines per se, while the disadvantage was felt by those who hoped for some synthesis, some formulation, or some agreement on a finite set of perspectives on the future of marine biology.

The ecological papers were introduced by K. M. Rae (Edinburgh), who examined the parameters of the marine environment that should be studied and was the first among many speakers to call for more intensive effort at culture of marine organisms. A. C. Redfield (Woods Hole) emphasized the inadequacy of experiments in marine biology and, thereby, opened a debate which continued as a thread through subsequent discussions. Papers by P. Drach (Paris), W. Weiser (Seattle), and R. Riedl (Vienna) attacked conceptual and practical aspects of field ecology. G. Thorson (Copenhagen) reported evidence of an enormously greater consumption of food by invertebrate predators than fish predators on the bottom communities in the North Sea and further of an ecologically crucial period of quiescence of these invertebrate predators coinciding with the period of chief larval settlement of the common prey species. D. P. Wilson (Plymouth) described the present information on the selection of substratum by planktonic larvae ready for metamorphosis and on trace organic substances in certain water masses which promote the growth of larvae.

H. Barnes (Millport) illustrated a paper on the future of underwater television with startlingly detailed and revealing photographs of present-day achievements. Individual spines of echinoids and single zooplankters could be clearly seen. C. M. Yonge (Glasgow) opened a discussion on the physiology and ecology of reef-building corals and concluded with the opinion that algae, associated with the coral, are not of direct nutritional benefit to the coral. Others, and especially E. P. Odum (Athens, Ga.) felt that, in the light of recent discoveries, this question must be reopened.

V. and L. Tonolli (Pallanza, Italy) demonstrated the irregularities of distribution of plankton communities in fresh waters as measured by a continuously recording and sampling device that receives plankton through a plastic tube extending to the surface from the plankton net at 70 meters depth. A different and already classical form of continuous plankton recorder was one of the bases of a paper by A. C. Hardy (Oxford) emphasizing the possibilities of prediction of fishery conditions in the sea. Although the ecological papers as a whole showed great vitality in dealing with special cases, there was a complaint by some that an over-all accounting for the distribution of organic matter and the flux of energy, as between major fractions of the living mass and of the nonliving reservoirs, was not being faced up to.

The series of biochemical and physiological papers was begun by E. Baldwin (London) and continued by T. H. Bullock (Los Angeles), E. S. Guzman Barrow (Chicago), and A. Szent-Gyorgyi (Woods Hole) whose essay entitled "Motion, energy transmission and the cellular matrix," proposed a new theory of the linkage between energy-releasing mechanisms in muscle and the contractile portions of the protein. Ending up a heady day of provocative new ideas, C. S. Pittendrigh (Princeton) and F. A. Brown (Evanston, Ill.) reported experiments on a wide range of organisms analyzing rhythms of daily, tidal, and lunar periodicity.

S. K. Kon (Reading, England) documented the tortuous path of the scientist with a story of the search for vitamin A in bathypelagic organisms which began in a dairy research institute. W. Rodhe (Uppsala) thrilled all those who hope for intensive work on productivity of natural waters by recounting recent experiences with daily C^{14} measurements in a Swedish lake, and R. Margalef (Barcelona) followed with a complementary report on close-grained analysis of temporal succession and spatial heterogeneity in occurrence of phytoplankton. D. I. Arnon (Berkeley) and L. Provasoli (New York) pointed up the opportunities and difficulties in the study of inorganic micronutrients and organic growth factors.

Behavior and its mechanisms formed the common denominator of three contributions by W. H. Thorpe (Cambridge), T. H. Waterman (Yale), and A. D. Hasler (Madison, Wis.), the latter two suggesting new or little understood sensory modalities as the basis for navigation and migration.

The series of contributions in the area of evolution and population genetics included several reports on successful experiences in the breeding and culturing of species of marine invertebrates, especially those by V. L. Loosanoff (Milford, Conn.) on pelecypods, and D. L. Ray (Seattle) on crustaceans, polychaetes, and other groups, and W. Matsui (Kyoto) on the pearl oyster. Problems of speciation in the sea and of the influence of breeding structure of the population were discussed by W. Wieser (Seattle), C. Barigozzi (Milan), and A. J. Kohn (Honolulu).

Moving in closer, A. Novick (Chicago) cited experiments with continuous-flow-culture techniques on bacteria permitting experimental observation of evolutionary processes in response to imposed changes in the environmnt. R. A. Lewin (La Jolla) examined genetics in marine algae, and G. Montalenti (Naples) discussed sex determination in marine species. Moving back again for the broad look, P. Drach eloquently pleaded that marine biology not be studied as a special branch but simply as a favorable place for the examination of the most general problems of biology.

A notable experiment in conference technique sent groups of eight or ten participants selected for diversity into daily sessions of almost unstructured discussion. The six different so-called "idea groups" had, as might be expected, very different experiences, but it was commonly reported that at least some of the time fruitful discussions resulted.

It was a matter of general regret that four Russian delegates, who were expected until the last minute, cabled their apologies. The proposal by Zenkevich to include a biological program of field work in the International Geophysical

Year was endorsed by a vote of the symposium.

Methods were a frequent topic. Severe criticism of long-accepted techniques, criticisms for failure to use available techniques or to standardize those in use, and suggestions for new methods, ranging from ingenious simplified procedures, such as Margalef's "diversity indices" to genuinely imaginative large-scale attacks on the problems, both of data procurement and data reduction by automatic processes commensurate with the size and complexity of the problems in the seas, were rife. Beyond techniques, there was a strong feeling continually coming to the surface that classical approaches, especially to ecology, are inadequate in the recognition of the criteria of the environment to be measured. As a single example of this, many were impressed by the new field of micro- and even ultramicronutritional factors affecting marine populations.

One ecologist said, "I felt that ecology is rapidly coming to occupy a strong position as a 'bridger of gaps' between physical sciences and the experimental biologist who has been the 'fair-haired child' for the past decade. What scares me is that ecology is not well prepared in terms of manpower and sound modern research know-how to fulfill this important role." A minor persistent theme was the strategy of science. Two views that were expressed surprised some in their incompatibility and in the prominence of the issue in other peoples' thinking. A clear majority seemed firmly in favor of absolute freedom of activity for the research worker, even though this means that an institute of oceanography would not have a theme, let alone a definite project. A minority felt that, especially in the science of the sea, some limitation of objectives is essential and that it might be better in marine biology to have more engineers even if it means having fewer scientists.

The papers, together with submitted discussions, are being edited for publication by the University of California Press.

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Cosmic Distance Scale

Our knowledge of the universe depends basically on astronomical distances. The accuracy of the determination of distances presents a major challenge to astronomers. The need of a critical review and a fresh look at this complex problem prompted this Conference on the Cosmic Distance Scale, which was sponsored by the National Science Foundation and the Leander McCormick Observatory of the University of Virginia. The conference was held 5–7 Apr. 1956 at Charlottesville, where 30 participants and invited guests were present. Two foreign astronomers were invited, but, of these, only Otto Heckmann (Hamburg) was able to attend. Daniel Chalonge (Institut d'Astrophysique, Paris) met with last minute visa difficulties and was unable to be present [*Science* **124**, 127 (20 July 1956)]. However, his contribution was read.

All proceedings were tape-recorded, because it is our aim to publish the papers as well as much of the discussion. The first day was devoted to astrometry, the second to spectroscopic determinations of distances, and the third to extragalactic distances of the nearby nebulae.

Our knowledge of the distances of the stars in our immediate neighborhood is based on geometric considerations. The most fundamental method of determining these distances, that of trigonometric parallaxes, makes use of the earth's orbit around the sun. Even for stars within 150 light-years of the sun, we are confronted with serious limitations in accuracy of this method. The nature of the systematic errors present is still unknown. In addition, this geometric method provides distances relative to the background stars only. From the motion of the distant stars, absolute distances are obtained, which, in turn, add to our uncertainties. Among the suggestions for remedying the situation were the establishment of a southern station with a telescope exactly like the 20-inch astrograph of the Lick Observatory for the determination of the motion of the stars in the southern sky and the construction of a large reflector designed especially for the determination of distances by means of geometric methods. Another geometric method uses the sun's path through space as a base line for distance determinations. This method is mainly of statistical value, producing mean distances for certain types of stars. It is affected by uncertainties in the assumed relative motions of stars in various parts of our stellar system.

By establishing the intrinsic luminosity of a star and by comparing it with the star's apparent luminosity, the star's distance is derived. The spectrum of a star yields the star's intrinsic luminosity, provided that we know from geometric or kinematic considerations the distance of a number of stars for calibration purposes. Therefore, the uncertainties of the previous determinations are, by necessity, included in this method of determination. This is particularly true for stars of high luminosity that are at great distances. Here enters, also, the uncertainty owing to the interstellar absorption of the light received from the stars. However, it appears possible to take this into account by measuring the reddening of the light owing to the interstellar particles.

The nearby clusters provide an independent method for calibrating our spectra and securing luminosities. The line-of-sight velocities of the stars in a cluster and their projected motions on the sky yield the distance to the cluster. It was shown that the distance of the Hyades is the most accurately known distance among the clusters. But, since the members of this cluster do not include stars of all luminosities and spectral types, the stars of other clusters suitably superimposed on the calibration line of stars of the Hyades are used. It was pointed out that, in order to do this, it is necessary to know the ages of the different clusters, since evolutionary changes of the stars affect their luminosity. Here again we are confronted with new uncertainties.

The well-known method of determining distances by means of the intrinsic luminosities of Cepheid variables is more complicated than it was originally thought to be. This method utilizes the relationship between the period of light variation and the intrinsic brightness of these stars. However, this period-luminosity relationship is not unique for all kinds of Cepheid variables. Five "families" of Cepheid variables have been identified from independent considerations, and, for each of these, a relationship period and luminosity seems to exist.

The final session of the conference dealt with the determination of the distances of the nearby external galaxies. The distance indicators of these objects are stars similar to some kinds of stars that we find in our stellar system. By necessity, they must be of high luminosity and, at the same time, identifiable with certainty with their counterparts in our own system. Much of this work is now in progress. The expressed opinion was that it will take a number of years to complete. But, in spite of all the precautions that are taken, a 25-percent accuracy in their distances will be difficult to attain.

The problem of the distant galaxies, of which no individual stars are visible, was not discussed. Its solution will depend on the clarification of our present difficulties and uncertainties.

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Meeting Notes

■ The first of a series of annual symposia on naval hydrodynamics will be held in Washington, D.C., 24–28 Sept. It will be sponsored by the mechanics branch of

the Office of Naval Research, in cooperation with the National Academy of Sciences–National Research Council. The papers will survey critically the various areas of hydrodynamics that are basic to Naval and marine applications.

The program for the symposium includes the following speakers: C. C. Lin, on boundary layer stability; S. Corrsin, on turbulence in shear flows; G. K. Batchelor, on wave scattering owing to turbulence; M. J. Lighthill, on river waves; W. H. Munk and M. Tucker, on the ocean wave spectrum; D. Gilbarg, on free streamline theory and steady-state cavitation; M. S. Plesset, on physical effects in cavitation and boiling; H. Snay, on hydrodynamics of underwater explosions; G. P. Weinblum, on seaworthiness; H. Lerbs, on hydrodynamics of marine propulsion; J. V. Wehausen on ship wave phenomena; M. Strasberg, and H. M. Fitzpatrick, on hydrodynamic noise; J. B. Parkinson, on hydrodynamics of water-based aircraft; J. W. MacColl and R. N. Cox, on basic hydroballistic phenomena; and J. C. Niedermair, on hydrodynamic barriers in ship design.

For further information write to John S. Coleman, National Academy of Sciences–National Research Council, Washington 25, D.C.

■ The Committee on Geographic Pathology of the Research Commission of the International Union against Cancer, of which Harold L. Stewart (National Institutes of Health) is chairman, has planned three meetings to study the problems of cancer in Africa. The first is a symposium on cancer of the liver to be held 24–31 Aug. in Kampala, Uganda, East Africa. The tentative program includes (i) definition of the terms *cirrhosis, necrosis, fatty change, kwashiorkor,* and *primary cancer* of the liver; (ii) experimental necrosis, regeneration, and fibrosis of liver; (iii) world distribution, kwashiorkor, infectious hepatitis, cirrhosis, and cancer of the liver; (iv) pathology of kwashiorkor, cirrhosis, cancer of the liver and experimental cancer of the liver; (v) mechanism of chemical carcinogenesis of the liver of the rat; (vi) clinical aspects, diagnosis, and therapy of kwashiorkor, cirrhosis, cancer of the liver, endocrinological aspects of liver disease; (vii) liver function tests and alteration in metabolism in patients with cirrhosis; (viii) nutritional and physiological aspects of liver disease; (ix) enzyme activity of rat liver during carcinogenesis; (x) enzyme activity of hepatic tissue in kwashiorkor.

It is hoped that this symposium in Kampala will afford the opportunity for scientists from different parts of the world to meet, to examine one another's material, to have an exchange of ideas with the view to improving the knowledge of liver disease and cancer in Africa and to stimulating new studies along these lines. It is anticipated that there will be approximately 27 participants, representing ten countries. This meeting is being generously supported by the British Empire Cancer Campaign, the Medical Research Council, and the Colonial Office, and by the cancer organizations in the countries from which the delegates are coming.

Immediately following the meeting in Kampala most of the participants will continue on to a meeting arranged for 1–5 Sept. in Leopoldville, Belgian Congo. This meeting is being supported by the Louvanian University, Leopoldville, and the Belgian Government. The meeting in Leopoldville will be on a broader scale than that of Kampala and will consider not only all forms of cancer in Africa but also all forms of cancer in relation to other diseases, geography, race, and so forth. There will be specialized presentations on the geography of Africa south of the Sahara. There will be a special presentation regarding the characteristics of the different ethnic groups that inhabit this area. Cancer in the African Negro will be discussed in relation to cancer in other races. Nutrition, avitaminosis, siderosis of the liver, peptic ulcer, and parasites will be discussed in relation to cancer and to other diseases. A central repository for pathological specimens from Africa will be considered. A large part of the program will be devoted to consideration of methods for the collection of statistical data within stated geographic limits. Toward the end of the symposium, time will be set aside to consider what problems for research can be recommended for study in Africa.

Immediately following the meeting in Leopoldville, several of the participants will go on to Dakar, French West Africa, to accept the invitation by the Haut Commissaire of the Government of the French Republic in West Africa, to study the types of cancer and related diseases that may be observed in the hospitals of Dakar. M. Payet is organizing the meeting in Dakar. Those accepting the invitation, numbering around 12 individuals, will be guests of the Governor General. The meetings will include visits to the Native Central Hospital, to the Principal Hospital, and to the Institut Pasteur. A side trip a little distance from Dakar will take the group to the Nutritional Study Center to observe the work in progress there. The main meetings will be held at the Medical School in Dakar.

■ The fall general meeting of the American Institute of Electrical Engineers, to be held 1–5 Oct., in the Morrison Hotel, Chicago, Ill., will honor the centenary of the birth of Nikola Tesla, the inventor of the alternating-current motor. Commemorating Tesla's contributions to the electric industry, Samuel G. Hibben will deliver a demonstration lecture on Tesla's work related to high-frequency studies connected with radiation or luminous phenomena.

Fifty-four technical sessions are scheduled. The six technical divisions of the institute (communications, general applications, industry, power, science, and electronics and instrumentation) will hold symposia and sessions on developments in their fields. The institute's committee on management will present a panel discussion by several young graduate engineers, who will discuss their formal education, their training on the job, and the opportunities offered them. Those attending the meeting have also been invited to the 12th annual Electronics Conference, which will be held 1–3 Oct., in the Sherman Hotel, Chicago.

■ The third annual convention of the Society of Nuclear Medicine has been held in Salt Lake City. Eight regional groups interested in the application of radioactive isotopes to biology and medicine were inducted as chapters. Three days were devoted to papers on almost every aspect of medicine involved in the use of isotopes. There were also scientific and commercial exhibits.

■ The Atmospheric Optics Symposium, sponsored by Boston University Physical Research Laboratories, will be held at Sargent Camp, Peterborough, N.H., 5–7 Sept. It will be devoted to atmospheric problems in aerial photography, the photography of celestial and airborne objects, and vision through the atmosphere. For information write to F. Dow Smith, Director, Boston University Physical Research Laboratories, 700 Commonwealth Ave., Boston 15, Mass.

■ The second national symposium on Aeronautical Communications, which is being sponsored by the Professional Group on Communications Systems of the Institute of Radio Engineers, will be held in Utica, N.Y., 8–10 Oct. There will be four open sessions on communications systems and components, and two sessions classified confidential on military data links and long-range communications.

■ The third annual meeting of the Professional Group on Nuclear Science of the Institute of Radio Engineers will be held in Pittsburgh, Pa., at the Mellon Institute and Hotel Webster Hall, 20–22 Sept. The program will include sessions on nuclear science, computation and simulation, instrumentation, and reactor control. For information write to James B. Callaghan, Westinghouse Bettis Plant-W3R-N, P.O. Box 1468, Pittsburgh 30, Pa.

■ The third annual East Coast Conference on Aeronautical and Navigational Electronics will be held 29–30 Oct. in Fifth Regiment Armory, Baltimore, Md. The conference is jointly sponsored by the Baltimore chapter of the Institute of Radio Engineers, the Professional Group on Aeronautical and Navigational Electronics, and the electronics industry. Nearly 2500 engineers, scientists and industrial representatives are expected to attend the technical program and industrial exhibition during the 2-day meeting.

■ A symposium on optics and microwaves will be held at Lisner Auditorium of George Washington University, Washington, D.C., 14–16 Nov. The meeting is jointly sponsored by the Professional Group on Antennas and Propagation of the Institute of Radio Engineers, George Washington University, and the Optical Society of America. The technical program of six sessions is designed for scientists in the fields of engineering, medicine, and related physical sciences whose work concerns optical phenomena. In addition, survey papers will be presented to aid understanding of the basic physics underlying optics and microwaves.

■ The 22nd North American Wildlife Conference will be held 4–6 Mar. 1957 at the Statler Hotel in Washington, D.C. Papers for presentation at one of the six technical sessions should be sent to the appropriate chairman *before 15 Nov.* The sessions and their chairman are: disease, nutrition, and controls, O. Wilford Olsen (Colorado Agricultural and Mechanical College, Fort Collins); wetlands and inland water resources, Frank C. Bellrose, Jr. (Illinois Natural History Survey, Urbana); upland game resources, Wendell G. Swank (Arizona Game and Fish Department, Phoenix); marine and coastal resources, Clarence P. Idyll (Marine Laboratory, University of Miami, Coral Gables, Fla.); big game resources, Harold S. Crane (Utah Fish and Game Commission, Salt Lake City); conservation education, John D. Bulger (National Wildlife Federation, Rt. 2, Groton, N.Y.).

Forthcoming Events

September

10–12. **American Soc. of Mechanical Engineers, fall, Denver, Colo.** (C. E. Davies, ASME, 29 W. 39 St., New York 18.)

10–12. **Electron Microscope Soc. of America, annual, Madison, Wis.** (Miss J. R. Cooper, Nela Park 130, Cleveland 12, Ohio.)

10–12. **Information Theory, symposium, Cambridge, Mass.** (P. Elias, Massachusetts Inst. of Technology, Cambridge 39).

10–14. **Electron Transport in Metals and Solids, colloq., Intern. Union of Pure and Applied Physics, Ottawa, Canada.** (K. C. MacDonald, National Research Council, Ottawa.)

10–14. European Soc. of Cardiology, 2nd cong., Stockholm, Sweden. (K. E. Grewin, Sodersjukhuset, Stockholm.)

10–14. Immunomicrobiological Standardization Symposium, 2nd, Rome, Italy. (G. Penso, Instituto Superiore di Sanita, Viale Regina Elena, 299, Rome.)

10–14. International Conf. on Fatigue of Metals, London, England. (Secretary, Institution of Mechanical Engineers, 1, Birdcage Walk, Westminster, London, S.W.1.)

10–14. International Cong. on Catalysis, Philadelphia, Pa. (H. Heinemann, ICC, c/o Houdry Process Corp., P.O. Box 427, Marcus Hook, Pa.)

10–14. International Cong. of Dietetics, 2nd, Rome, Italy. (American Dietetic Assoc., 620 N. Michigan Ave., Chicago 11, Ill.)

10–15. High-Speed Photography, 3rd intern. cong., London, England. (Congress Secretariat, Dept. of Scientific and Industrial Research, Charles House, 5–11 Regent St., London, S.W.1, England.)

10–15. Perkin Centennial, New York, N.Y. (A. G. Bruinier, Jr., E. I. Du Pont de Nemours & Co., P.O. Box 386, Wilmington 98, Del.)

13–16. International Rorschach Soc., 3rd cong., Rome Italy. (Secretary, IRS, 6, Fischerweg, Bienne, Switzerland.)

13–17. Static Electricity in Textiles, Zurich, Switzerland. (General Secretary, Textile Institute, 10 Blackfriars St., Manchester 3, England.)

14–15. Calorimetry Conf., 11th annual, Baltimore, Md. (H. A. Boorse, Pupin Physics Laboratories, Columbia Univ., New York 27.)

15–22. Congreso Panamericano de Gerontología, 1st, Mexico, D.F., Mexico. (E. V. Cowdry, Washington Univ. School of Medicine, St. Louis 10, Mo.)

15–23. Instruments and Measurements, 4th intern. conf. and exhibition, Stockholm, Sweden. (S. Malström, P. O. Box 36, Stockholm 12.)

16–21. American Chemical Soc., Atlantic City, N.J. (A. H. Emery, ACS, 1155 16 St., NW, Washington 6.)

16–22. American Soc. for Testing Materials, Pacific Coast meeting, Los Angeles, Calif. (R. J. Painter, ASTM, 1916 Race St., Philadelphia 3, Pa.)

17–19. Alpine Meteorology, 4th intern. cong., Chamonix, France. (Dr. Piery, Institut de Meteorologie et des Sciences des Climats, 72 Rue Pasteur, Lyon, France.)

17–21. Illuminating Engineering Soc., annual, Boston, Mass. (A. D. Hinckley, IES, 1860 Broadway, New York 23.)

17–21. Instrument Soc. of America, 11th international conf., New York, N.Y. (F. J. Tabery, 250 W. 57 St., New York 19.)

17–21. Theoretical Physics, intern. cong., Seattle, Wash. (J. H. Manley, Dept. of Physics, Univ. of Washington, Seattle 5.)

17–22. International Astronomical Federation, 7th cong., Rome, Italy. (J. A. Stemmer, IAF, P. O. Box 37, Baden, Switzerland.)

17–23. European Confederation of Agriculture, 8th general assembly, Sheveningen, Netherlands. (M. Collaud, ECA, Pestalozzistrasse 1, Brugg, Argovie, Switzerland.)

19–23. International Cong. of Internal Medicine, 4th, Madrid, Spain. (C. Jimenez Diaz, Facultad de Medicina, Madrid.)

20–21. Physical Chemistry of Processes at High Pressures, general discussion, Faraday Soc., Glasgow, Scotland. (F. C. Tompkins, Faraday Soc., 6 Gray's Inn Sq., London, W.C.1, England.)

21–22. Pharmacotherapy in Mental Illness, Washington, D.C. (J. O. Cole, National Research Council, 2101 Constitution Ave., NW, Washington 25.)

21–28. History of Medicine, 15th cong., Intern. Soc. for the History of Medicine, Madrid and Salamanca, Spain. (Luis S. Granjel, Instituto Arnaldo de Vilanova de Historia de la Medicina, Duque de Medinaceli, 4, Madrid.)

23–26. International Bureau of Differential Anthropology, 4th cong., San Remo, Italy. (Bureau International d'Athropologie Differentielle, Institut d'Anatomie de Université Ecole de Medicine, Geneva, Switzerland.)

24–25. Industrial Electronics Symposium, 5th annual, Cleveland, Ohio. (C. F. Schunemann, Thompson Products, 2196 Clarkwood Rd., Cleveland 3.)

24–26. American Oil Chemists' Soc., Chicago, Ill. (Mrs. L. R. Hawkins, AOCS, 35 E. Wacker Drive, Chicago 1.)

24–26. Biochemistry of Lignin, 3rd round table, Appleton, Wis. (H. F. Lewis, Inst. of Paper Chemistry, Appleton.)

24–27. Science of Photography, international conf., Cologne, Germany. (W. Schürmeyer, Hohenstaufenring 48/54, Cologne.)

24–28. **International Dairy Cong., 14th, Rome, Italy.** (R. E. Hodgson, Dairy Husbandry Research Branch, U.S. Dept. of Agriculture, Beltsville, Md.)

24–29. International Scientific Film Assoc., 10th cong., Vienna, Austria. (Secretariat of Intern. Assoc., 38, Ave. des Ternes, Paris 17, France.)

25–27. Atomic Industrial Forum and Trade Fair, 3rd annual conf., Chicago, Ill. (C. Robbins, AIF, 260 Madison Ave., New York 16.)

25–28. American Roentgen Ray Soc., annual, Los Angeles, Calif. (B. R. Young, Germantown Hospital, Philadelphia 44, Pa.)

25–28. Assoc. of Iron and Steel Engineers, annual, Cleveland, Ohio. (Secretary, AISE, Empire Bldg., Pittsburgh 22, Pa.)

25–29. Atmospheric Condensation Nuclei, 2nd intern. symp., Basel and Locarno, Switzerland. (M. Bider, Astronomical Meteorological Station, Basel, Switzerland.)

25–29. Automatic Controls, international conf., Univ. of Heidelberg, Germany. (R. Oldenburger, Woodward Governor Co., Rockford, Ill.)

26–28. The Direction of Research Organizations, intern. symp. Teddington, England. (National Physical Laboratory, Teddington, Middlesex, England.)

26–28. **Mississippi Valley Medical Soc., annual, Chicago, Ill.** (H. Swanberg, 510 Maine St., Quincy, Ill.)

(See issue of 20 July for comprehensive list)

Kodak reports to laboratories on:

non-hygroscopic acetylcholine iodide . . . a better chance of getting through to the besieged brain . . . recruiting talent for high-energy physics

A delightful business

You sit one fine morning reading your mail and lo, there is a letter from a researcher at a medical school in the green hills of Vermont who wants to know why you don't put up acetylcholine as the quaternary iodide. Somehow, possibly by reading it in a book, he seems to have learned that acetylcholine iodide is not hygroscopic at all, whereas that well known vasodilator acetylcholine itself and its well known bromide (Eastman 2117) absorb so much water from the air that to try to weigh them out accurately is a nuisance. There doesn't seem to be a solitary reason in the world why you can't put up acetylcholine iodide. You even think of a way to make it from starting material less costly than acetylcholine. You try it and it works and the iodide *is* non-hygroscopic. That particular researcher is pleased at what an agreeable fellow you are, and you are pleased at the prospect of all the acetylcholine iodide that all the other researchers are going to buy from you.

So now all you have to do is to advertise that Acetylcholine Iodide (*Eastman 7209*) *costs $2.60 for 10 g. and is one of some 3500 highly purified organic chemicals sold by Distillation Products Industries, Eastman Organic Chemicals Department, Rochester 3, N. Y.* (*Division of Eastman Kodak Company*).

Movies with comment

As between 55 pages of typescript to detail the progress on a certain project for last month and six minutes of Kodachrome movies to do the same, which has the better chance of getting through to the besieged brain?

Since you can't say everything without words and since you have to be quite rich to afford a full-dress sound movie that is looked at once or twice and filed for the record, you use a magnetically recorded commentary. At the time we process the film for your dealer (and you can, if you wish, specify us as your favorite color film processor), we can lay down a *Kodak Sonotrack Coating* along the edge. While the *Kodascope Magnetic-Optical Sound Projector* shows the picture, appropriate extending remarks are spoken into the microphone. Any remarks that seem less than appropriate when the projector plays them back with the picture have merely to be respoken. Automatically the boo-boo is wiped clean and replaced by wiser words.

This projector we have just brought out now. We hadn't thought it wise to take anybody's money for such a machine until enough organizations had used our design without trouble and had liked the way it sounds.

From Eastman Kodak Company, Cine-Kodak Equipment Sales, Rochester 4, N. Y., one may expect an honest attempt at collaboration on sensible procedures for using inexpensive sound movies in technical communication and documentation.

Little black tracks

Rochester, a city which gets a fair amount of its living from the photographic emulsion, has been the site for the past six years of great international conferences on nuclear particle physics. It is mere coincidence that photographic emulsions are the source of much of the raw data that the savants come to trade, ponder, and debate. Yet, because we make some of the photographic emulsion they use, we are perhaps more awed than our butchering, baking, and candlestick-making fellow-townsmen at the mighty intellectuality focussed on the microscopic tracks of black specks that mark the births, encounters, and deaths of nucleons,

leptons, mesons (light and heavy), and hyperons. Here men and women strain every known resource of thought and mathematics to build a logical structure strong enough to hold these "elementary" particles until next year's conference, when parts of it will surely come crashing down as new evidence is presented.

Not the least remarkable aspect of this is the virtual certainty that here and there in the land there must be a kid (now in Cub Scouts or possibly trying to understand rock 'n' roll) who, a few years from now, will be reading the proceedings of these conferences with a smile of tolerance for the pitiful errors of the physicists who preceded him. A parent or teacher who suspects he knows such a kid has a chilling responsibility.

Scientific American *recently carried an article, "The Tracks of Nuclear Particles," pitched at those who have no knowledge of the subject or its vocabulary but who are blessed with vigorous, inquiring minds. We have bought 2,000 reprints to give away. Requests should be addressed to Eastman Kodak Company, Professional Goods Division, Rochester 4, N. Y.*

Price quoted is subject to change without notice.

This is one of a series of reports on the many products and services with which the Eastman Kodak Company and its divisions are . . . *serving laboratories everywhere*

Kodak
TRADE MARK

Equipment News

All inquiries concerning items listed here should be addressed to Science, *Room 604, 11 W. 42 St., New York 36, N.Y. Include the name(s) of the manufacturer(s) and the department number(s).*

■ MICROPHOTOMETER measures from 20 μμlu to 20 lu and indicates percentage of transmission, density, and phototube current directly. Three light-scattering cells are furnished with the instrument. These include a square cell (path length, 2.4 cm) for use in density, transmission, absolute turbidity, and 90° measurements; a cylindrical cell for use at scattered angles from 0° to 147°; and a microcell assembly for use when the same continuous angular measurements on samples no larger than 2.5 cm^3 are made. Optical transmission from 10^{-9} to 100 percent is measurable. (American Instrument Co., Dept. S5)

■ LIGHT MODULATOR delivers pulses of light in the microsecond range and modulated beams that are variable from direct current to video frequencies. A crystalline analog of a Kerr cell that is made up of a Z-cut plate of ammonium or potassium dihydrogen phosphate is situated between electrodes and allows light to pass in the same direction as the applied electric field. For normally incident collimated light, the unit has the properties of a polarization retardation plate, with the magnitude of retardation directly proportional to the applied voltage. A beam can be modulated in intensity in accordance with the voltage applied to frequencies beyond the video region when the crystal device is placed between polarizers. (Baird Associates, Inc., Dept. S2)

■ SURFACE-QUALITY METER makes automatic and recorded measurements of gloss, haze, transmittance, reflectance, color, and other spectral values related to specific geometric conditions of illumination and view. Several different types of exposure heads may be used with the instrument. These include reflectometers, gloss heads, a transmittometer, a goniophotometer, and a hazemeter. A typical exposure head contains a light source, a comparison photocell, and a test photocell. The sample under examination is inserted in the head near the test photocell and is illuminated by light from the standard source, focused on it by lenses and mirrors. This illuminating light is reflected to the test cell. The exposure head is connected to the photometric unit. A zero adjustment compensates for stray light within the exposure head and is used to produce a zero reading on the dial when there is no sample in the sample area. The recorder can be made to record the values printed on the standard supplied. (Gardner Laboratory, Inc., Dept. S23)

■ NEUTRON MONITOR is a portable, battery-operated survey meter for the measurement of thermal and fast neutron fluxes of from 10 to $10^4/cm^2$ sec. The instrument contains two boron trifluoride proportional counters, one of which measures thermal neutrons. The other is sensitive only to neutrons with energies above the cadmium resonance at 0.176 ev. No response is given in the pure gamma flux of up to 100/mr hr. Fluxes of less than 10 neutron/cm^2 sec can be estimated. The meter scale is logarithmic and covers a range of from 10 to 10^4 neutron/cm^2 sec. (Nuclear Instrument and Chemical Corp., Dept. S19)

■ LABORATORY GLASSWARE is described in a recently published 52-page catalog. Listed are extractors, columns, pipettes, manometers, pumps, flasks, burettes, and chlorine, drying, gas-analysis, and distilling apparatus. (Delmar Scientific Co., Dept. S15)

The Market Place

BOOKS • SERVICES • SUPPLIES • EQUIPMENT

DISPLAY: Rates listed below — no charge for Box Number. Monthly invoices will be sent on a charge account basis—provided that satisfactory credit is established.

Single insertion	$22.00 per inch
13 times in 1 year	21.00 per inch
26 times in 1 year	20.00 per inch
52 times in 1 year	19.00 per inch

For PROOFS on display ads, copy must reach SCIENCE 4 weeks before date of issue (Friday of every week).

BOOKS AND MAGAZINES

PROFESSIONAL SERVICES

SUPPLIES AND EQUIPMENT

SUPPLIES AND EQUIPMENT

INCREASED CHARGE FOR STAIN CERTIFICATION

The Board of Trustees of the Biological Stain Commission announces an increase in the price of Certification Labels by 5¢ effective 1 Sept. 1956. This will result in a change from the current charge of 15¢ to a new charge of 20¢ per bottle to the purchasers of Certified Stains. This price increase has been necessitated by increasing costs in the operation of the Commission and is the first increase in almost 20 years.

The MARKET PLACE

BOOKS • SERVICES • SUPPLIES • EQUIPMENT

SUPPLIES AND EQUIPMENT

SUPPLIES AND EQUIPMENT

SUPPLIES AND EQUIPMENT

PERSONNEL PLACEMENT

CLASSIFIED: 18¢ per word, minimum charge $3.60. Use of Box Number counts as 10 additional words.

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Single insertion	**$22.00 per inch**
13 times in 1 year	**21.00 per inch**
26 times in 1 year	**20.00 per inch**
52 times in 1 year	**19.00 per inch**

For PROOFS on display ads, copy must reach SCIENCE 4 weeks before date of issue (Friday of every week).

POSITIONS WANTED

Biochemist, Ph.D.; group leader research and development. Experience protein chemistry, enzymes, isolation natural products, microbiology, and organic synthesis. Publications, patents. Box 192, SCIENCE. X

Biophysicist, Ph.D.; 6 years' research, university department experimental pathology; trained radioisotopes. Medical Bureau (Burneice Larson, Director), Palmolive Building, Chicago. X

Entomologist, Ph.D., 43; experience in taxonomy, teaching, research, faunistic survey, and curatorial work; desires change. Prefer non-industrial position. Box 181, SCIENCE. 8/17

Microbiologist, Ph.D.; teacher of all phases of microbiology, 3 years; industrial research and consultant experience; specialty biochemistry applied to food and agriculture. Statistical analyst. Publications. East. Currently employed, available 1 September. Box 197, SCIENCE. X

Microbiologist, Ph.D.; 17 years' university experience in bacteriology, biochemistry, and phytopathology. Desires challenging opportunity. Box 196, SCIENCE. 8/24; 9/7

Mycologist, Ph.D. 1942; background of chemistry, biochemistry, and plant sciences; 14 years' experience in fermentation and recovery work; 10 years' supervisory experience. Primary interest in developing fermentation products. Desires research; $15,000. Box 195, SCIENCE. X

Nurse, Ed.D.; 13 years' experience nursing service and education. Desires deanship or directorship university school of nursing; prefers new or developing program. Box 193, SCIENCE. 8/17, 24, 31

POSITIONS WANTED

Research and Teaching (pharmacotherapeutics, oral diagnosis), **Writing and Editing,** 9 years' extensive experience. Desires opportunity in research, writing, teaching, administrative (or combination) capacity. Age 33; family. Box 194, SCIENCE. X

POSITIONS OPEN

ANATOMY DEPARTMENT, DALHOUSIE UNIVERSITY. Applications are invited for an assistant professor in the Department of Anatomy. Experience in teaching and research in embryology and histology, or in neuroanatomy, is essential, and a working knowledge of gross anatomy is desirable. Candidates with a medical degree will be preferred, although those with an honors degree in medical science or biology will receive special consideration. The minimum salary for a medical graduate will be $5000. The salary will depend on qualifications and experience. Applications to be made to Professor R. L. deC. H. Saunders, Dalhousie University, Halifax, Nova Scotia, Canada. 6/8; 7/13; 8/10

Bacteriological Technician, small diagnostic laboratory. Newly remodeled air-conditioned building. Southwest. Box 188, SCIENCE. X

Biochemist experienced in natural product isolation to be project leader in laboratory of a large midwestern pharmaceutical company with expanding research program. Send résumé to Box 190, SCIENCE. 8/17

(a) Immunologist, Ph.D. or M.D.; competent teacher, interested research; faculty appointment, medical school with extensive expansion program; East. **(b) Medical Science Writer;** duties include surveying literature for technical staff and promotional department, pharmaceutical company; man required; $7000–$10,000. **(c) Scientists with Research Administration Backgrounds,** experienced research on etiology, pathogenesis, and therapy of cancer; interesting administrative positions. **(d) Biochemist,** Ph.D., experienced protein chemistry, enzyme work; hospital research department; $9000. S8-2, Medical Bureau (Burneice Larson, Director), Palmolive Building, Chicago. X

Research Assistant, sanitary chemistry. Half-time study toward graduate degree in Department of Preventive Medicine and Public Health. Contact Director, Staff Personnel, University of Texas–Medical Branch, Galveston, Texas. X

Research Microbiologist. Minimum of 6 years required in either an industrial or academic capacity. A good background in immunology and biochemistry required. Ph.D. preferred, but will consider M.S. Salary open. Inquire of Dr. Earl B. Gerheim, Sherman Laboratories, 5031 Grandy, Detroit 11, Michigan. 8/10, 17, 24, 31

POSITIONS OPEN

Pharmacologists—Ph.D.

Established Research Division of growing Pharmaceutical Company has immediate opportunities for pharmacologists with experience and training in:

1) CNS drug research. Work will involve general pharmacological screening and development of pharmacological testing methods.
2) Cardiovascular research. Work will involve design and supervision of screening procedures and development of basic research program.

Company has modern research facilities, complete employee benefit program and is located in rural area of central New York State. Forward résumés to Personnel Director, The Norwich Pharmacal Company, Norwich, New York.

Physical Chemist. Organic-Physical Ph.D., 30–35, to head group of investigators on long-range fundamental research problems of food technology in western Pennsylvania research institution. Soundly good future for right man who possesses leadership. Give full details of education, experience, salary requirements in first letter. Box 182, SCIENCE. 8/3, 10

POSITIONS REQUIRING DEGREES IN MEDICINE OR SCIENCE: (a) Chemist; Ph.D., 1 to 2 years' experience protein purification; work collaboratively with biology group, separation of biologically active pituitary proteins; $5600–$7800; also **(b) Research Assistant;** recent Ph.D. trained biochemistry, nutrition and/or endocrinology; collaborate on nutrition research program, especial interest vitamin-hormone interrelations; $4500–$5200; well-known Pacific Coast university. **(c) Bacteriologist;** degree, experience required; direct state public health laboratory, full administrative responsibility; $6120; residential city near large university medical center; Southeast. **(d) Organic Chemist;** Ph.D. to work on synthesis directed toward finding new medicinally valuable compounds; $7200 up; well-known eastern pharmaceutical concern. **(e) Biochemist;** M.A. or Ph.D.; approved 150-bed general hospital; $6000 up; lovely southern community. **(f) Research Ph.D.'s;** specialists in microbiology, immunology, virology, bacteriology, and pathology; principally virus research with view to new product development, related activities; concern engaged in manufacture, production of veterinary biologics, vaccines, and serums; $6000–$10,000; Midwest. Woodward Medical Personnel Bureau, 185 North Wabash, Chicago. X

Research Assistant, Biochemical Research. Permanent position in medical research institute. Detroit area. Will train applicant in enzyme and protein chemistry. B.S. or M.S. with chemistry or biochemical laboratory experience. Starting salary, $3600 to $4800, depending on qualifications. Send résumé and names of previous employers. Box 189, SCIENCE. X

APPLICATION FOR HOTEL RESERVATIONS

123rd AAAS MEETING

New York City, December 26-31, 1956

The list of hotels and their rates and the reservation coupon below are for your convenience in making your hotel room reservation in New York. Please send your application, *not* to any hotel directly, but to the AAAS Housing Bureau in New York and thereby avoid delay and confusion. (Members of the American Astronomical Society who wish reservations at uptown hotels should correspond directly with the Hayden Planetarium.) The experienced Housing Bureau will make assignments promptly; a confirmation will be sent you in two weeks or less. **As in any city, single-bedded rooms may become scarce; double rooms for single occupancy cost more; for a lower rate, share a twin-bedded room with a colleague.** Most hotels will place comfortable rollaway beds in rooms or suites at 2.50 or 3.00 per night. Mail your application *now* to secure your first choice of desired accommodations. All requests for reservations must give a definite date and estimated hour of arrival, and also probable date of departure.

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

Rates for Rooms with Bath*

All hotels have sessions in their public rooms. For a list of headquarters of each participating society and section, please see *Science*, July 20, or *The Scientific Monthly* for August.

Hotel	Single	Double Bed	Twin Bed	Suite
Governor Clinton	$7.00–11.00	$10.00–13.00	$11.00–17.00	$20.00–35.00
Martinique	5.00– 9.00	8.00–14.00	8.00–14.00	16.00–38.00
New Yorker	7.00–10.00	10.00–14.00	11.50–17.00	25.00 and up
Sheraton-McAlpin	6.75– 9.75	9.75–12.75	10.75–13.75	20.00 and up
Statler	8.00–12.00	11.00–15.00	11.50–18.00	31.00–33.00

* Subject to 5% New York City tax on hotel rooms.

---------- **THIS IS YOUR HOUSING RESERVATION COUPON** ----------

AAAS Housing Bureau
90 East 42nd Street
New York 17, N. Y.

Date of Application .....

Please reserve the following accommodations for the 123rd Meeting of the AAAS in New York City, Dec. 26–31, 1956:

TYPE OF ACCOMMODATION DESIRED

Single Room ..... Desired Rate ..... Maximum Rate .....

Double-Bedded Room ..... Desired Rate ..... Maximum Rate ..... Number in party .....

Twin-Bedded Room ..... Desired Rate ..... Maximum Rate .....

Suite ..... Desired Rate ..... Maximum Rate ..... Sharing this room will be:

(Attach list if this space is insufficient. The name and address of each person, including yourself, must be listed.)

.....

.....

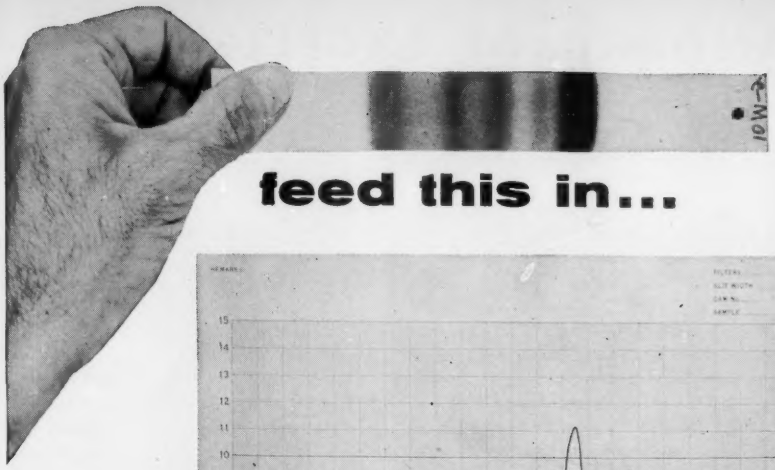
First Choice Hotel ..... **Second Choice Hotel** ..... **Third Choice Hotel** .....

DATE OF ARRIVAL ..... DEPARTURE DATE .....
(These must be indicated—add approximate hour, a.m. or p.m.)

NAME .....
(Individual requesting reservation) (Please print or type)

ADDRESS .....
(Street) (City and Zone) (State)

Mail this now to the Housing Bureau. **Rooms will be assigned and confirmed in order of receipt of reservation.**



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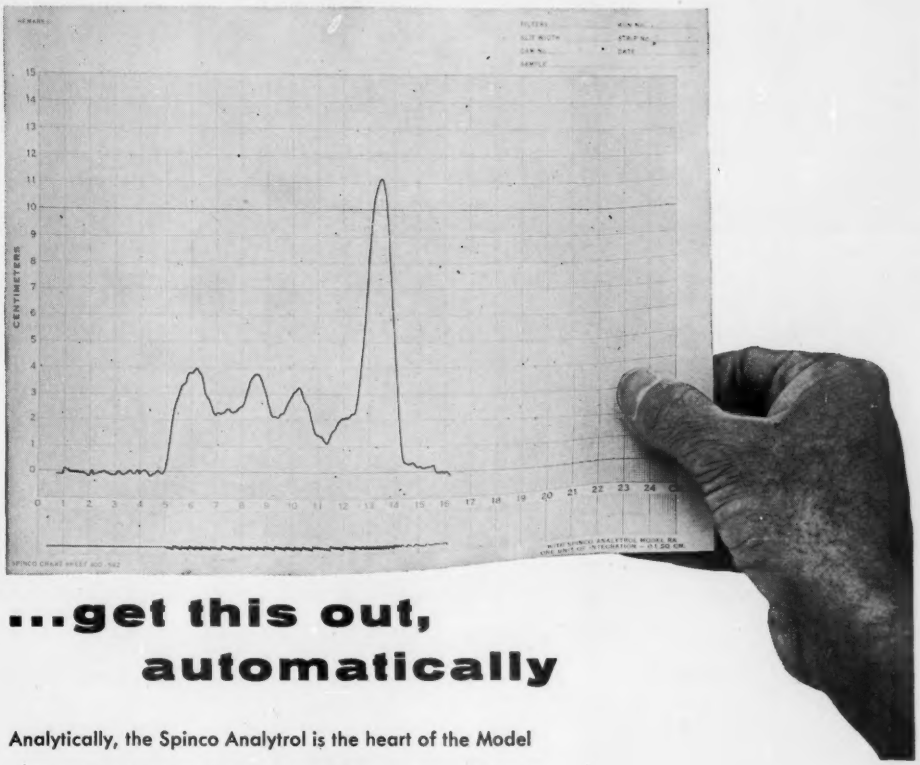

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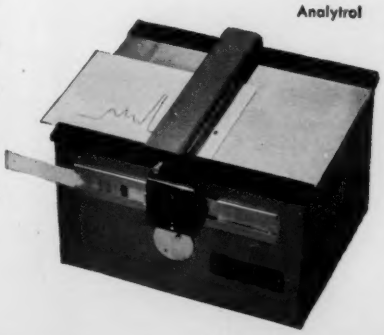
Analytically, the Spinco Analytrol is the heart of the Model R *Paper Electrophoresis System*, offering many additional advantages as a general laboratory tool.

In a matter of seconds it plots the distribution curve of material concentration derived from light transmission. At the same time, it produces an integral, saw-tooth curve from which relative concentrations can be read directly.

Model R Systems are stocked by distributors in principal cities. Or, write for details on this versatile instrument.

Spinco Analytrol



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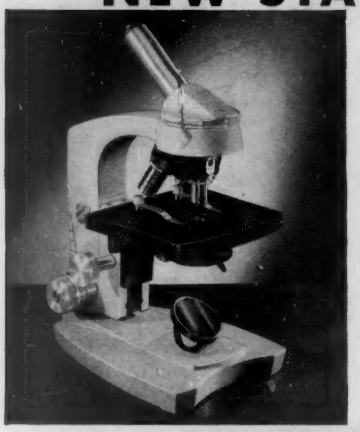
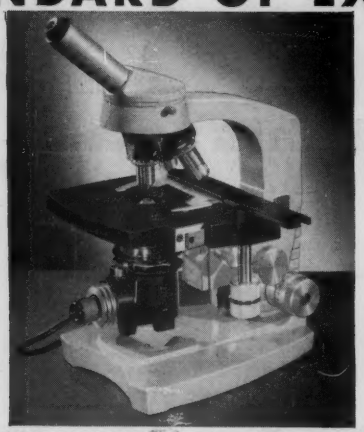
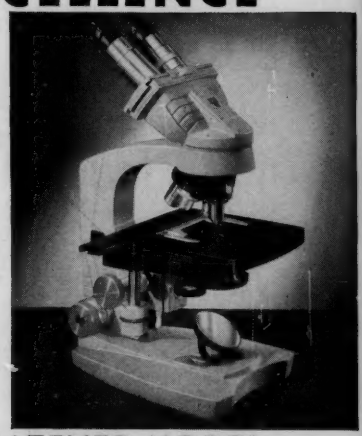

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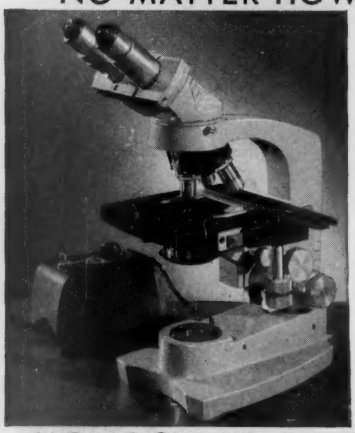
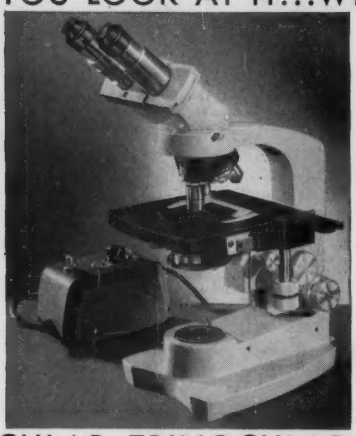
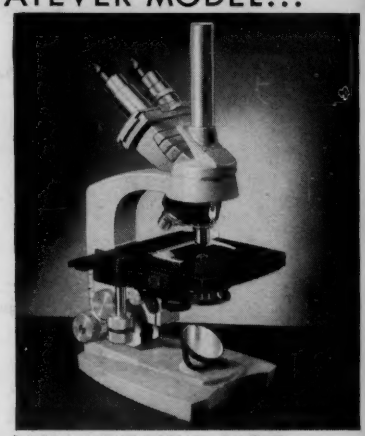

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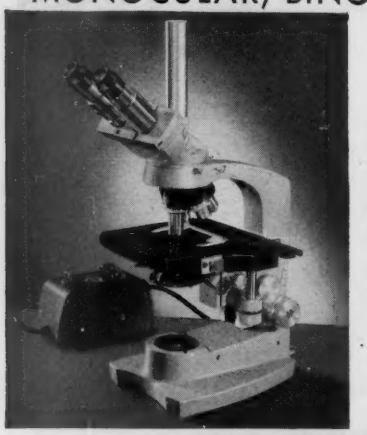
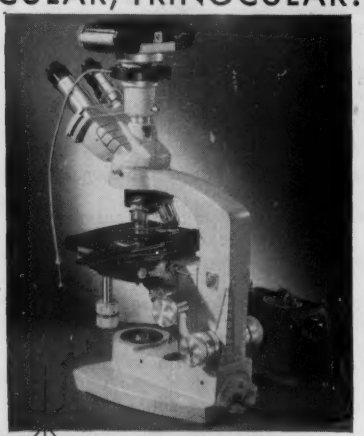
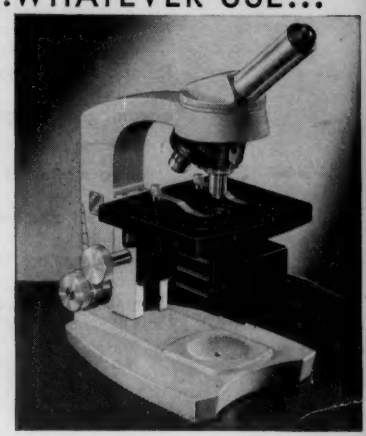

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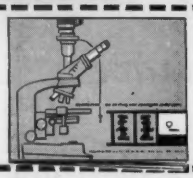

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